

Fig.1.

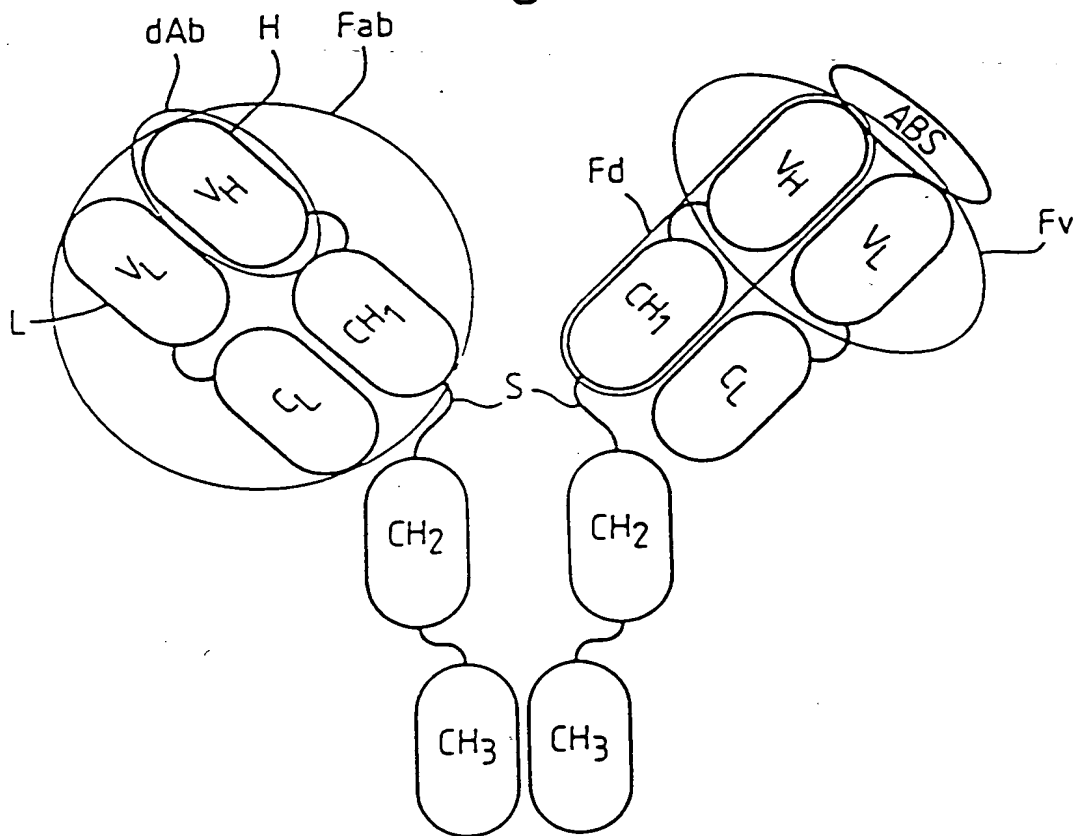


Fig.2 (i).

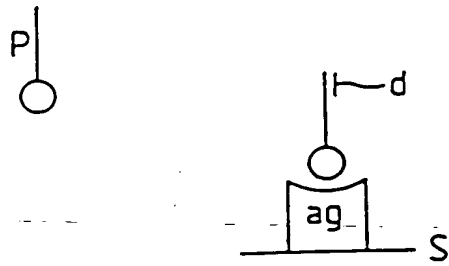


Fig.2 (ii).

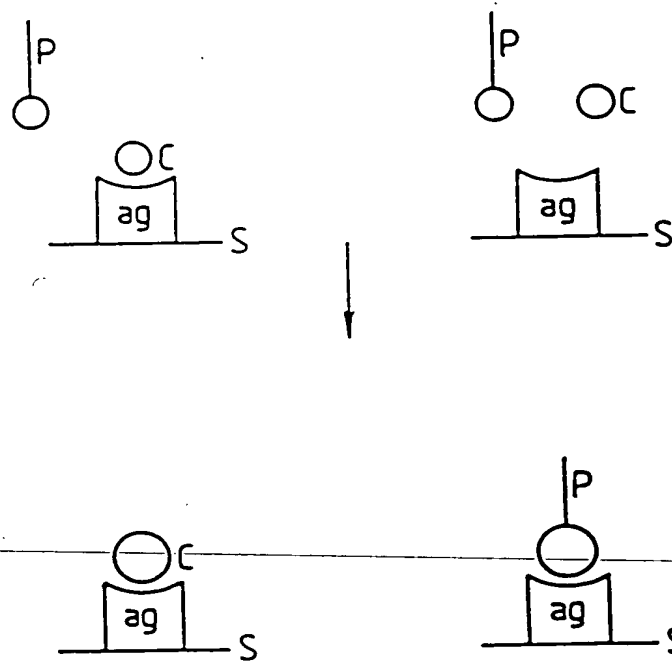
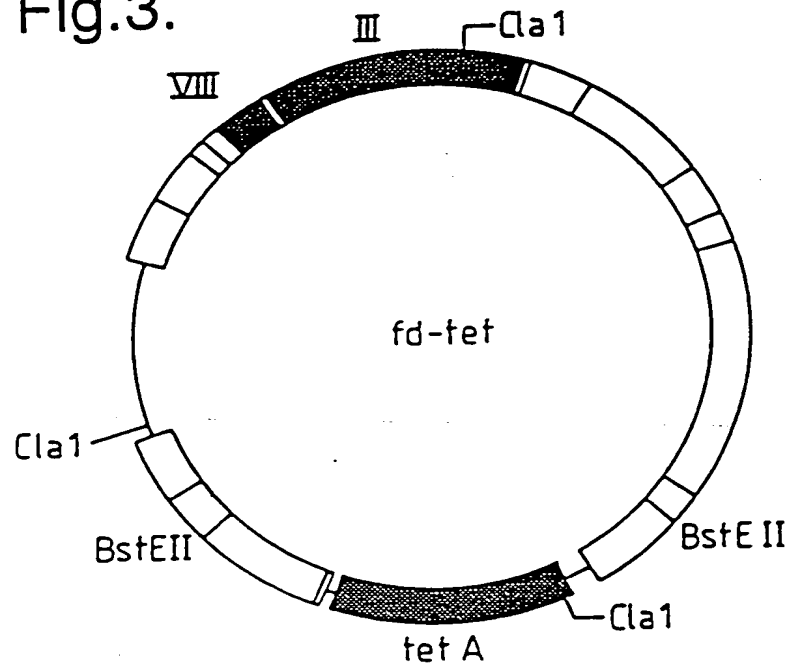


Fig.3.



fd - tet

~

cleave with BstEII

~

fill in with Klenow

~

re-ligate

↓

FDT6Bst

~

in vitro mutagenesis (oligo 1)

↓

FDTs/Bs

~

in vitro mutagenesis (oligo 2)

↓

FDTs/Xh

Fig.4 (i).

Oligo 1	(1653) ACA ACT TTC AAC AGT TGA GGA GAC GGT GAC CGT AAG CTT CTG CAG TTG GAC CTG AGC (SEQ ID NO. 177) GGA GTG AGA ATA (1620)
Oligo 2	(1653) ACA ACT TTC AAC AGT TTC CCG TTT GAT CTC GAG CTC CTG CAG TTG GAC CTG (SEQ ID NO. 178)
Oligo 3	(1704) GTC GTC TTT CCA GAC GTT AGT (SEQ ID NO. 179)

GENE III

SIGNAL  
CLEAVAGE SITE

Fig.4 (ii).

(1624) A TCT CAC TCC GCT	GAA ACT GTT GAA AGT (SEQ ID NO. 180)
Q V Q L Q (SEQ ID NO. 1) V T V S S (SEQ ID NO. 2)	
B TCT CAC TCC GCT CAG GTC CAA CTG CAG AAG CTT ACG GTC ACC GTC TCC TCA ACT GTT GAA AGT (SEQ ID NO. 181)	
	PstI BstEII
Q V Q L Q (SEQ ID NO. 1) L E I K R (SEQ ID NO. 3)	
C TCT CAC TCC GCT CAG GTC CAA CTG CAG GAG CTC GAG ATC AAA CGG GAA ACT GTT GAA AGT (SEQ ID NO. 182)	
	PstI XhoI

Fig.5.

rbs
M K Y L L P T A A  
GCATGCAAATTCATTTCAAGGAGACAGTCATAATGAAATACCTATTGCCTACGGCAGCC  
10
20
30
40
50
60

SphI                      pelB leader

A G L L L L A A O P A M A Q V Q L Q E S

GCTGGATTGTTATTACTGCTGCCCAACCGCGATGGCCCAGGTGCAGCTGCAGGAGTCA

70                      80                      90                      100                      110                      120

PstI

G P G L V A P S Q S L S I T C T V S G F  
GGACCTGGCCTGGTGGCGCCCTCAGAGCCTGTCCATCATGCACCGTCTCAGGGTTC  
130 140 150 160 170 180

S L T G Y G V N W V R Q P P G K G L E W  
TCATTAACCGGCTATGGTGTAACCTGGGTTCCGCCAGCCTCCAGGAAAGGGTCTGGAGTGG  
190 200 210 220 230 240

VHD1.3

L G M I W G D G N T D Y N S A L K S R L

CTGGGAATGATTTGGGGTGATGGAACACAGACTATAATTTCAGCTCTCAAATCCAGACTG

250 260 270 280 290 300

S I S K D N S K S Q V F L K M N S L H T  
AGCATCAGCAAGGACAACCTCCAAGAGCCAGTTTTCTTAAAAATGAACAGTCTGCACACT  
310 320 330 340 350 360

D D T A R Y Y C A R E R D Y R L D Y W G  
GATGACACAGCCAGGTA C T A C T G T G C C A G A G A G A G A T T A T A G G C T T G A C T A C T G G G G C  
370 380 390 400 410 420

Q G T T V T V S S G G G G S G G G S G  
 CAAGGCACCA~~CGGTCA~~CGGTCTCTCTCAgggtggaggcggttcaggcggaggtggctctggc  
 430 440 450 460 470 480  
 BstEII

G G G S D I E L T Q S P A S L S A S V G  
 ggtggcggaatcgGACATCGAGCTCACTCAGTCTCCAGCCTCCCTTTCTGCGTCTGTGGA  
 490 500 510 520 530 540  
 SacI

Fig.5 (Cont).

E T V T I T C R A S G N I H N Y L A W Y  
GAAACTGTCACCATCACATGTCGAGCAAGTGGGAATATTACAAATTATTTAGCATGGTAT  
550 560 570 580 590 600

Q Q K Q G K S P Q L L V Y Y T T T L A D  
CAGCAGAAACAGGGAAAATCTCCTCAGCTCCTGGTCTATTATACAACAACCTTAGCAGAT  
610 620 630 640 650 660

VKD1.3

G V P S R F S G S G S G T Q Y S L K I N  
GGTGTGCCATCAAGGTTTCAGTGGCAGTGGATCAGGAACACAATATTCTCTCAAGATCAAC  
670 680 690 700 710 720

S L Q P E D F G S Y Y C Q H F W S T P R  
AGCCTGCAACCTGAAGATTTTGGGAGTTATTACTGTCAACATTTTGGAGTACTCCTCGG  
730 740 750 760 770 780

Myc Tag (TAG1)

T F G G G T K L E I K R E O K L I S E E  
ACGTTCCGGTGGAGGGACCAAGCTCGAGATCAAACGGGAACAAAACTCATCTCAGAAGAG  
790 800 810 820 830 840

XhoI

D L N \* \* (SEQ ID NO. 183)

GATCTGAATTAATAATGATCAAACGGTAATAAGGATCCAGCTCGAATTC (SEQ ID NO. 184)  
850 860 870 880

EcoRI

Fig.6.

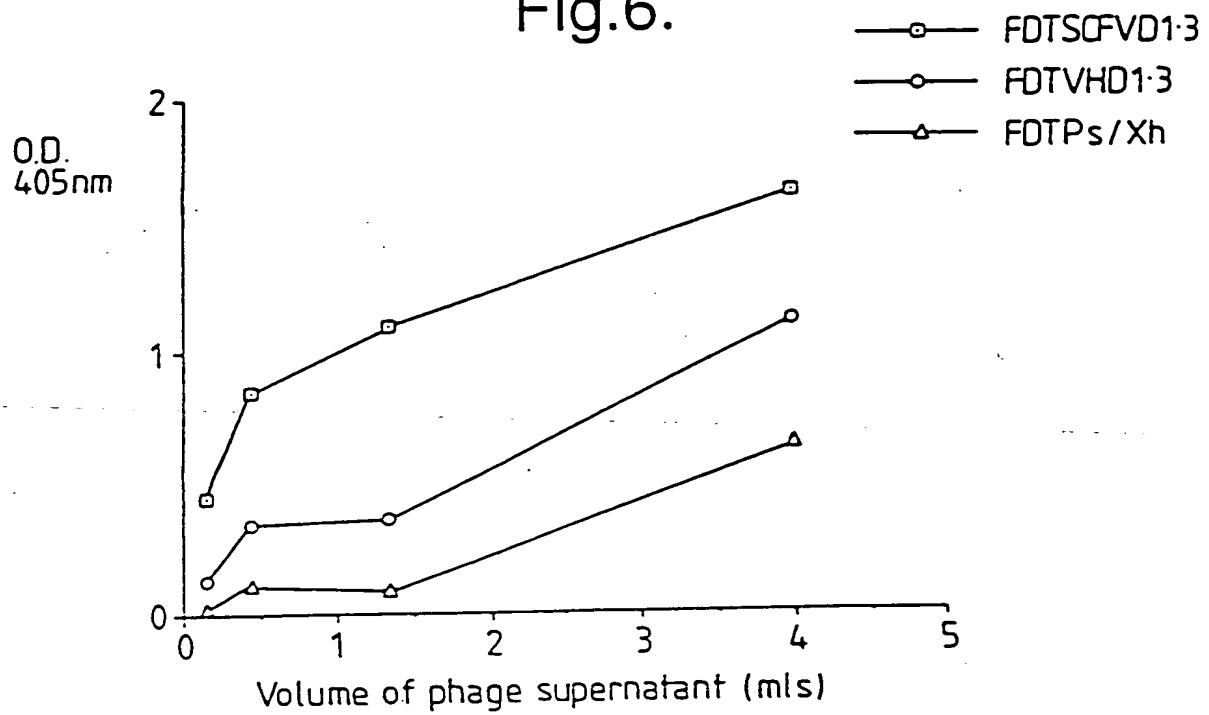


Fig.7.

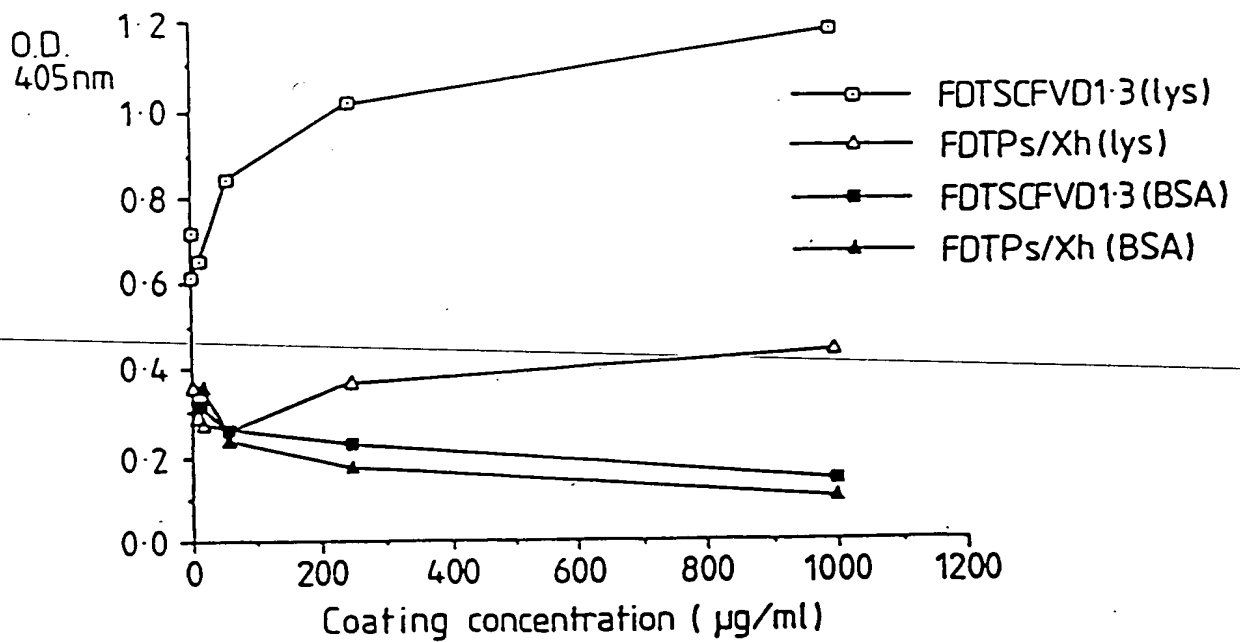


Fig.8.

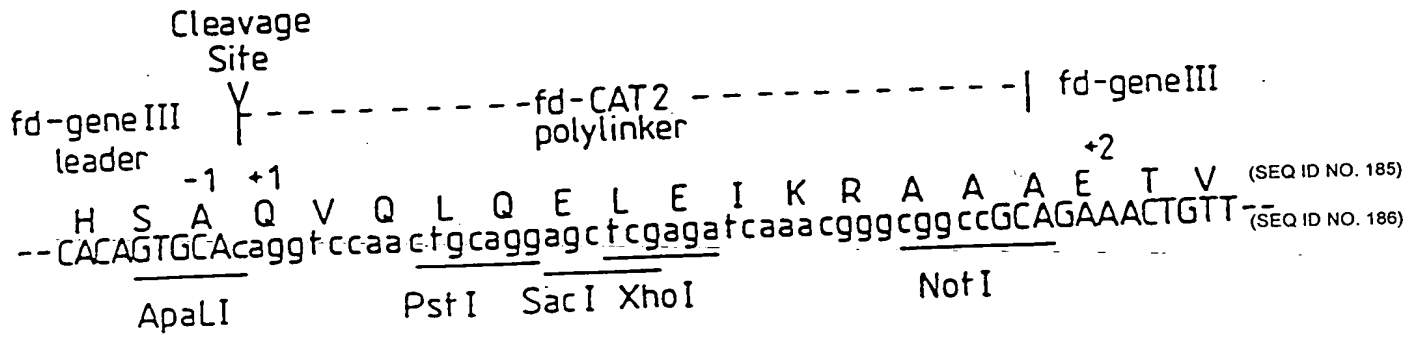


Fig.9.

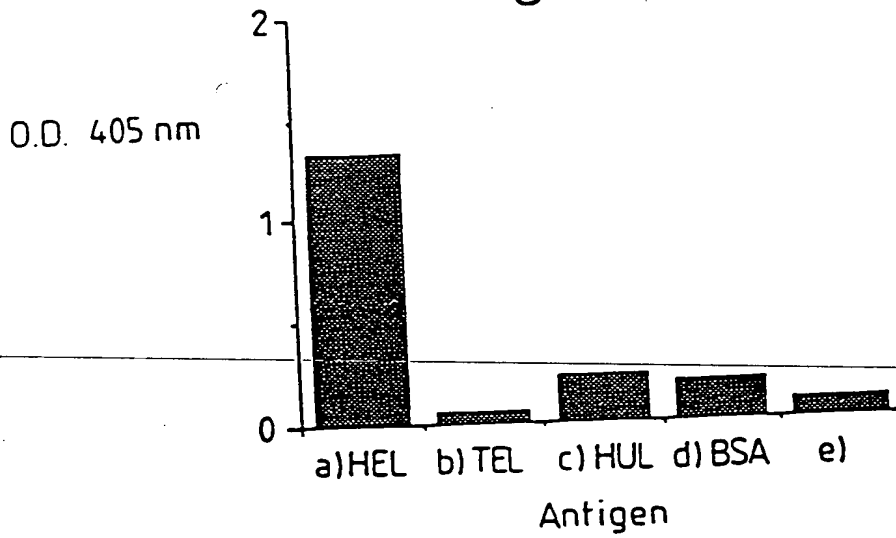




Fig.10.

M K Y L L P T A A  
GCATGCAAATTCTATTTC AAGGAGACAGTCATAATGAAATACCTATTGCTACGGCAGCC  
10 20 30 40 50 60

A G L L L L A A Q P A M A Q V Q L Q E S  
GCTGGATTGTTATTACTGCTGCCCAACCAGCGATGGCCCAAGGTCAGCTGCAGGAGTCA  
70 80 90 100 110 120

G P G L V A P S Q S L S I T C T V S G F  
GGACCTGGGCTGGTGGGGCCCTCAGAGCGCTGTCCATCACATGCACCGTCTCAGGGTTC  
130 140 150 160 170 180

S L T G Y G V N W V R Q P P G K G L E W  
TCATTACCGGCTATGGTGTAACTGGGTTCGCCAGCGCTCCAGGAAAGGGTCTGGAGTGG  
190 200 210 220 230 240

L G M I W G D G N T D Y N S A L K S R L  
CTGGGAATGATTGTTGGGGTIGATGGAACACAGACTATAATTACGCTCTCAAATCCAGACTG  
250 260 270 280 290 300

S I S K D N S K S Q V F L K M N S L H T  
AGCATCAGCAAGGACAACCTCCAAGAGCCAAGTTTTCTTAAAAATGAACAGTCTGCACACT  
310 320 330 340 350 360

D D T A R Y Y C A R E R D Y R L D Y W G  
GATGACACAGCCAGGTACTACTGTGCCAGAGAGAGAGATTATAGGCTTGACTACTGGGGC  
370 380 390 400 410 420

Q G T T V T V S S A S T K G P S V F P L  
CAAGGCACCAAGGTACCGTCTCCTCAGCGCTCCACCAAGGGCCCATGGGTCTTCCCCCTG  
430 440 450 460 470 480

A P S S K S T S G G T A A L G C L V K D  
GCACCCCTCCTCCAAGAGCACCTCTGGGGGCACAGGGGCCCTGGGCTGGTCAAGGAC  
490 500 510 520 530 540

Fig.10 (Cont 1).

Y F P E P V T V S W N S G A L T S G V H  
TACTTCCCCGAACCGGTGACGGTGTGGTGGAACTCAGGCGCCCTGACCAGCGGGGTGCAC  
550 560 570 580 590 600

T F P A V L Q S S G L Y S L S S V V T V  
ACCTTCCCGGCTGTCTACAGTCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTG  
610 620 630 640 650 660

P S S S L G T Q T Y I C N V N H K P S N  
CCCTCCAGCAGCTTGGGCAACCCAGACCTACATCTGCAACGTGAATCACAAGCCACGCAAC  
670 680 690 700 710 720

T K V D K K V E P K S S \* \* (SEQ ID NO. 187)  
ACCAAGGTGACAAAGAAAGTTCAGCCCAATCTTCATAATAACCCGGGAGCTTGCATGCA  
730 740 750 760 770 780

M K Y L L P T A A A G L  
AATTCTATTTCAAGGACACAGTCAATGAATAACCTATTGGCTACGGCAGCCGCTGGAT  
790 800 810 820 830 840

L L L A A Q P A M A D I E L T Q S P A S  
TGTTATTACTGGCTGGCCCAACCCAGGATGGCCGACATCGAGCTCACCAGTCTCCAGCCT  
850 860 870 880 890 900

L S A S V G E T V T I T C R A S G N I H  
CCCTTTCCTGGTCTGTGGGAGAAACGTGCACCATCAGATGTGGAGCAAGTGGGAATATT  
910 920 930 940 950 960

N Y L A W Y Q Q K Q G K S P Q L L V Y Y  
ACAATTATTTAGCATGGTATCAGCAGAAACAGGGAAATCTCCTCAGCTCCTGGTCTATT  
970 980 990 1000 1010 1020

Fig.10 (Cont 2).

T T T L A D G V P S R F S G S G S G T Q  
ATACAACAACCTTAGCAGATGGTGTGCCATCAAGGTTTCAGTGGCAGTGGATCAGGAACAC  
1030 1040 1050 1060 1070 1080

Y S L K I N S L Q P E D F G S Y Y C Q H  
AATATTCTCTCAAGATCAACAGCCTGCGAGCCTGAAGATTTTGGGAGTTATTACTGTCAAC  
1090 1100 1110 1120 1130 1140

F W S T P R T F G G G T K L E I K R T V  
ATTTTGGAGTACTCCTCGGACGTTGGTGGAGGCCACCAAGCTCGAGATCAAAACGGACTG  
1150 1160 1170 1180 1190 1200

A A P S V F I F P P S D E Q L K S G T A  
TGGCTGCAACCATCTGTCTTCATCTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAACTG  
1210 1220 1230 1240 1250 1260

S V V C L L N N F Y P R E A K V Q W K V  
CCTCTGTGTGTGTGCCCTGCTGAATAACTTCTATCCCAGAGAGGCCAAAGTACAGTGAAGG  
1270 1280 1290 1300 1310 1320

D N A L Q S G N S Q E S V T E Q D S K D  
TGGATAACGCCCTCCCAATGGGTAACTCCCAGGAGAGTGTCAACAGAGCAGGACAGCAAGG  
1330 1340 1350 1360 1370 1380

S T Y S L S S T L T L S K A D Y E K H K  
ACAGCACCTACAGCCTCAGCAGCAACCTGACGCTGAGCAAAGCAGACTACGAGAAACACA  
1390 1400 1410 1420 1430 1440

V Y A C E V T H Q G L S S P V T K S F N  
AAGTCTACGCCCTGGGAAGTCAACCATCAGGGCCTGAGCTGCGCCGTCACAAAGAGCTTCA  
1450 1460 1470 1480 1490 1500

R G E S \* \* (SEQ ID NO. 188)  
ACCGGGAGAGTCATAGTAAGAATTC (SEQ ID NO. 189)  
1510 1520

Fig.10 (Cont 3).

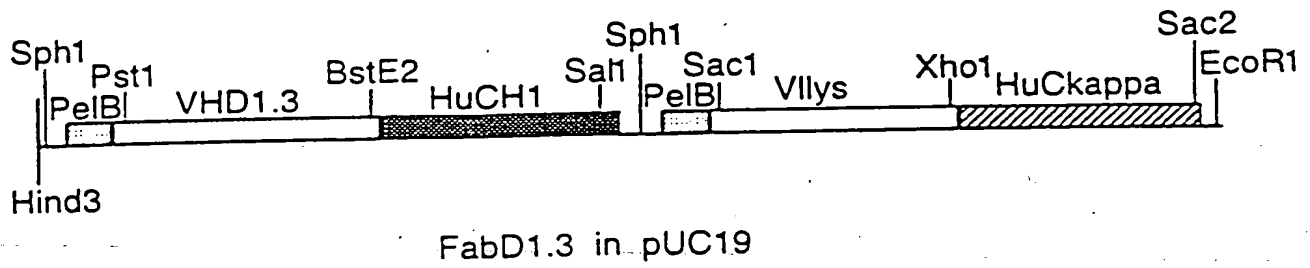


Fig.11.

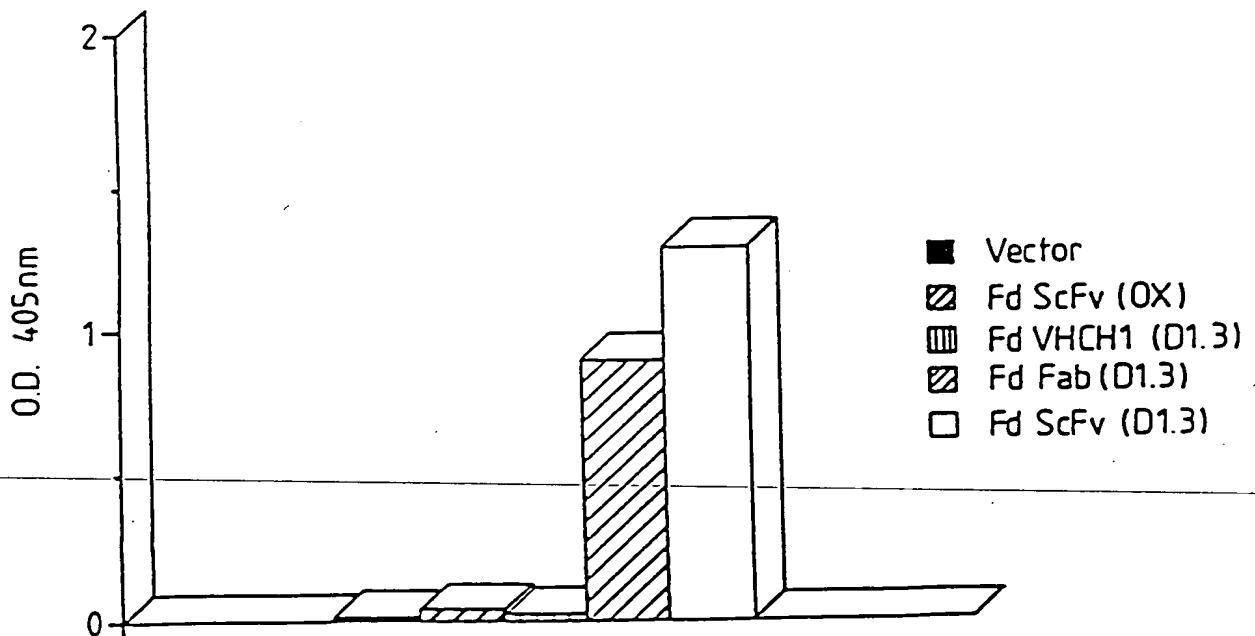


Fig.12a.

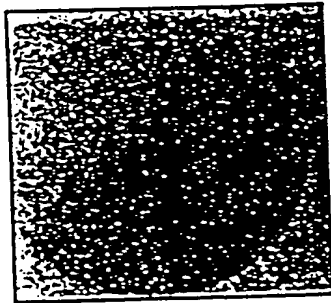


Fig.12b.

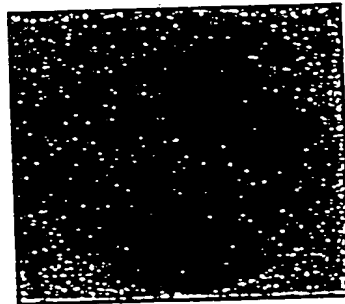


Fig.13.

Q V Q L Q E S G G G L V Q P G G  
 CAG GTG CAG CTG CAG GAG TCA GGA GGA GGC TTG GTA CAG CCT GGG GGT  
 PstI  
 S L R L S C A T S G F T F S N Y  
 TCT CTG AGA CTC TCC TGT GCA ACT TCT GGG TTC ACC TTC AGT AAT TAC  
 Y M G W V R Q P P G K A L E W L  
 TAC ATG GGC TGG GTC CGC CAG CCT CCA GGA AAG GCA CTT GAG TGG TTG  
 G S V R N K V N G Y T T E Y S A  
 GGT TCT GTT AGA AAC AAA GTT AAT GGT TAC ACA ACA GAG TAC AGT GCA  
 S V K G R F T I S R D N F Q S I  
 TCT GTG AAG GGG CGG TTC ACC ATC TCC AGA GAT AAT TTC CAA AGC ATC  
 L Y L Q I N T L R T E D S A T Y  
 CTC TAT CTT CAA ATA AAC ACC CTG AGA ACT GAG GAC AGT GCC ACT TAT  
 Y C A R G Y D Y G A W F A Y W G  
 TAC TGT GCA AGA GGC TAT GAT TAC GGG GCC TGG TTT GCT TAC TGG GGC  
 Q G T L V T v s s g g g g s g g g g s  
 CAA GGG ACC CTG GTC ACC gtc tcc tca ggtgggaggcggttcaggcgggagggtggctct  
 BstEII  
 g g g g s d i E L T Q T P L S L P V  
 ggcggtggcggtcggac atc GAG CTC ACC CAA ACT CCA CTC TCC CTG CCT GTC  
 SacI  
 S L G D Q A S I S C R S S Q S I  
 AGT CTT GGA GAT CAA GCC TCC ATC TCT TGC AGA TCT AGT CAG AGC ATT  
 V H S N G N T Y L E W Y L Q K P  
 GTA CAT AGT AAT GGA AAC ACC TAT TTA GAA TGG TAC CTG CAG AAA CCA  
 PstI  
 G Q S P K L L I Y K V S N R F S  
 GGC CAG TCT CCA AAG CTC CTG ATC TAC AAA GTT TCC AAC CGA TTT TCT  
 G V P D R F S G S G S G T D F T  
 GGG GTC CCA GAC AGG TTC AGT GGC AGT GGA TCG GGG ACA GAT TTC ACA  
 L K I S R V E A E D L G V Y Y C  
 CTC AAG ATC AGC AGA GTG GAG GCT GAG GAT CTG GGA GTT TAT TAC TGC  
 F Q G S H V P Y T F G G G T K L  
 TTT CAA GGT TCA CAT GTT CCG TAC ACG TTC GGA GGG GGG ACC AAG CTC  
 E I K R  
GAG ATC AAA CGG (SEQ ID NO. 190)  
 XhoI (SEQ ID NO. 191)

Fig.14.

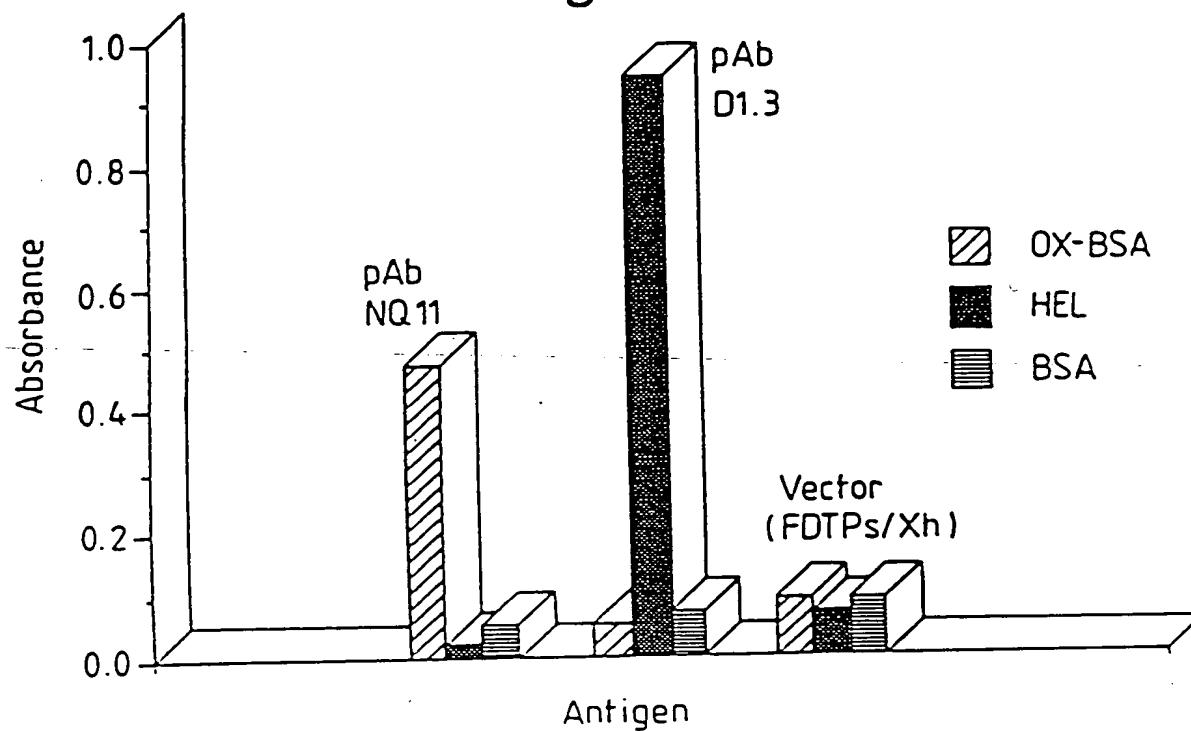


Fig.15.

5' END

TCT CAC AGT GCA CAA ACT GTT GAA CGG ACA CCA GAA ATG CCT GTT CTG (SEQ ID NO. 192)  
 TCT CAC AGT GCA CAA ACT GTT GAA CGG ACA CCA GAA ATG CCT GTT CTG (SEQ ID NO. 193)  
 ApaL1

3' END

K A A L G L K  
 AAA GCC GCT CTG GGG CTG AAA GCG GCC GCA GAA ACT GTT GAA AGT etc.  
 Not I

Fig.16 (i).

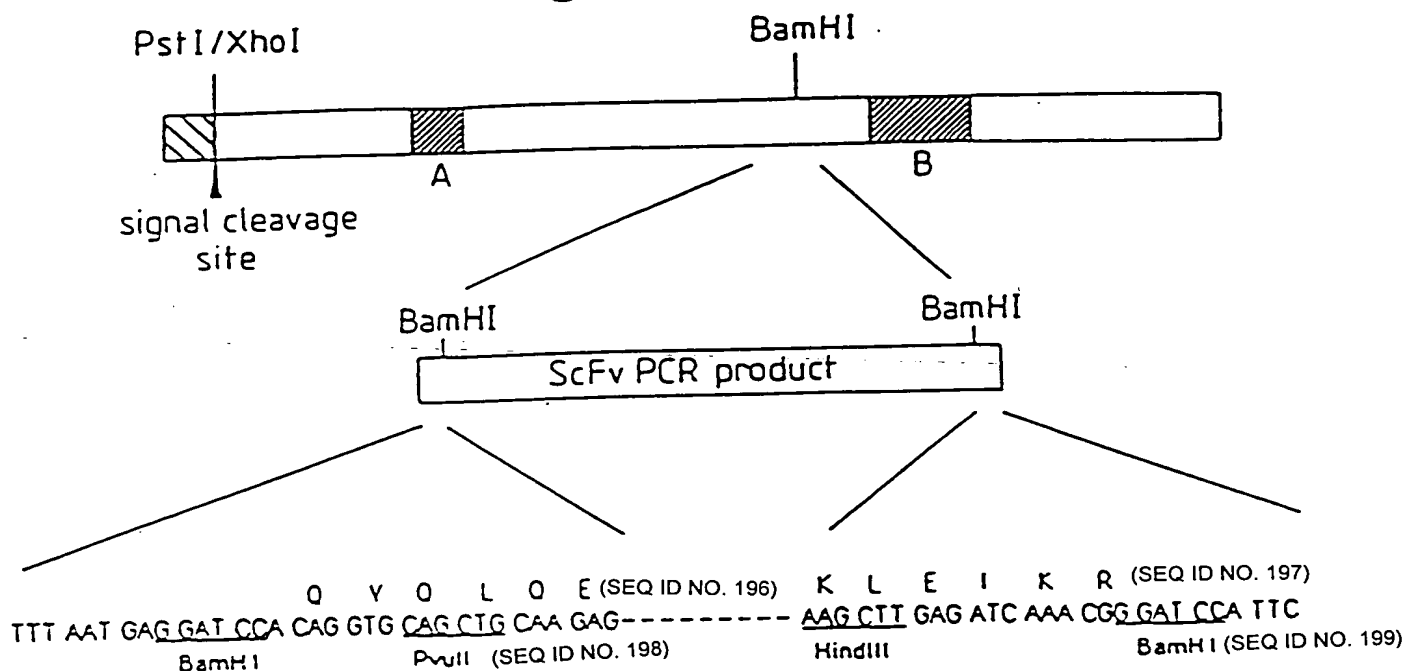


Fig.16 (ii).

A (1834) 5' GAG GGT GGT GGC TCT (SEQ ID NO. 200)

- - -C - - (SEQ ID NO. 201)

- - -C - - (SEQ ID NO. 202)

- - -C - ACT 3'(1839) (SEQ ID NO. 203)

B (2284) 5' - GGC GGC GGC TCT (SEQ ID NO. 204)

- GGT GGT GGT - (SEQ ID NO. 205)

- - GGC GGC - (SEQ ID NO. 206)

GAG - - GGC - (SEQ ID NO. 207)

- - - GGT - (SEQ ID NO. 208)

- - - GGC - (SEQ ID NO. 209)

- - - GGT - (SEQ ID NO. 210)

- - - GGC - 3'(2379) (SEQ ID NO. 211)

Reverse complement of mutagenic  
oligo G3Bamlink

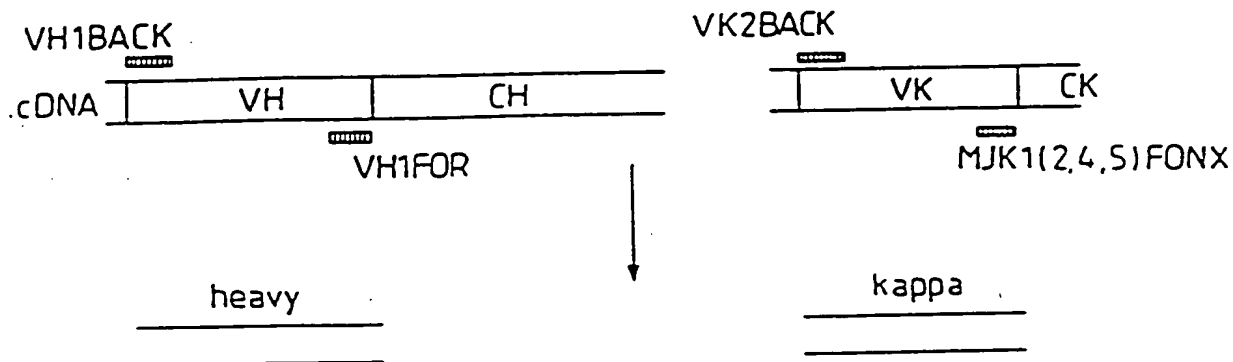
5' GAG GGT GGC GGA TCC (SEQ ID NO. 212)

GAG GGT GGC GG 3' (SEQ ID NO. 213)

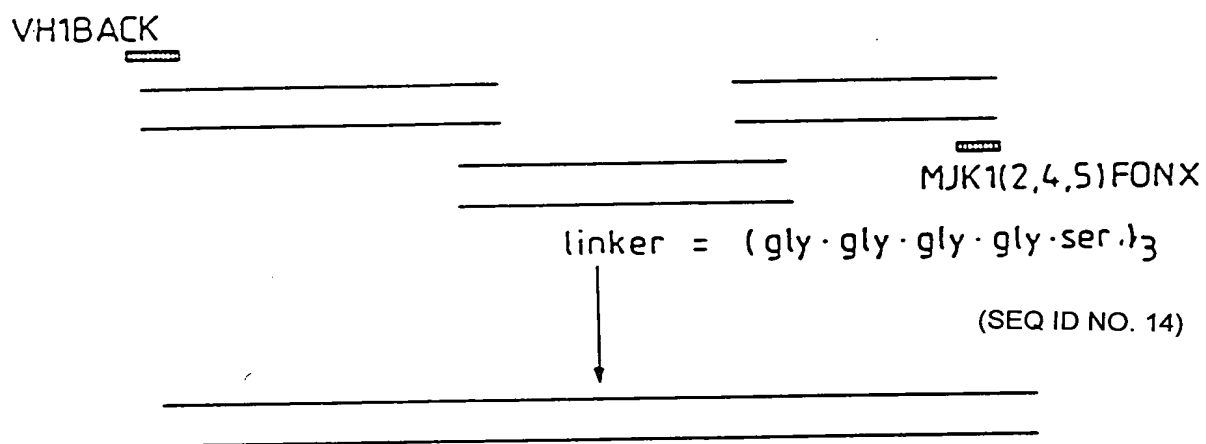


Fig.17.

1) PRIMARY PCR



2) ASSEMBLY PCR



3) ADDING RESTRICTION SITES

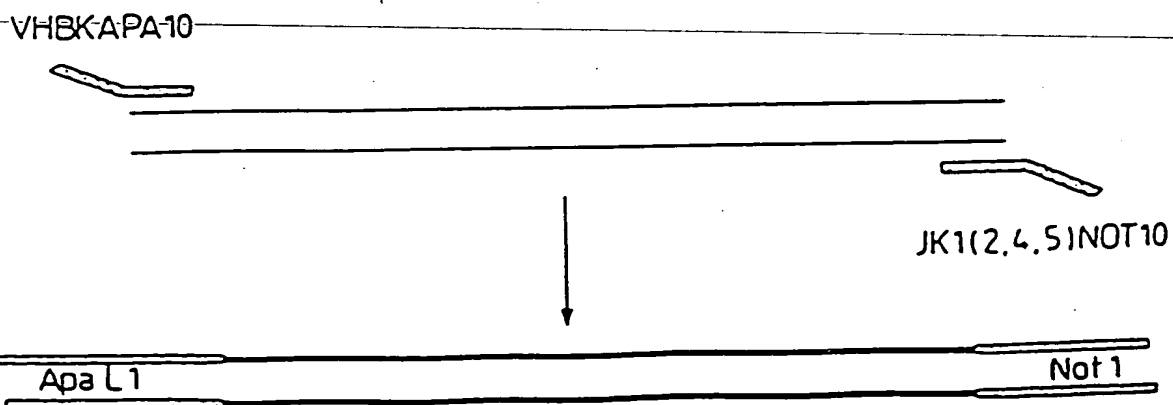


Fig.18.



Fig.19.

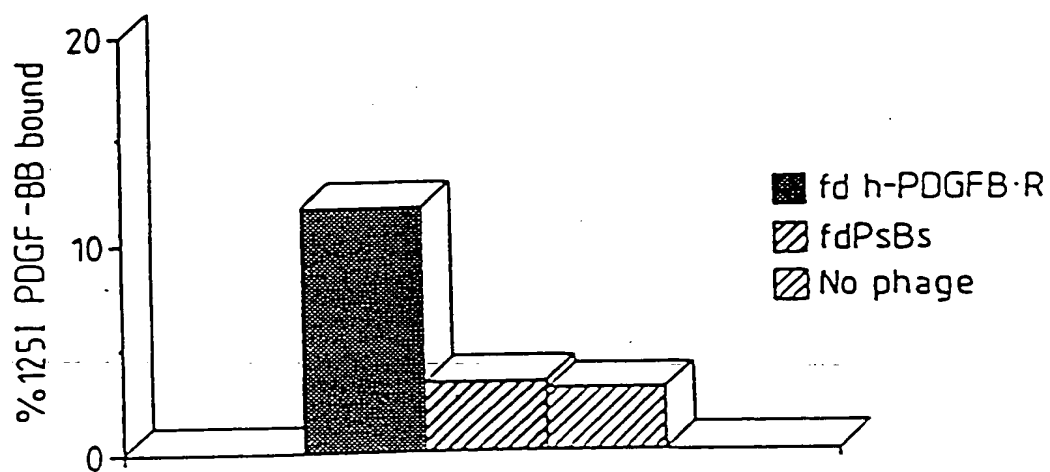


Fig.20.

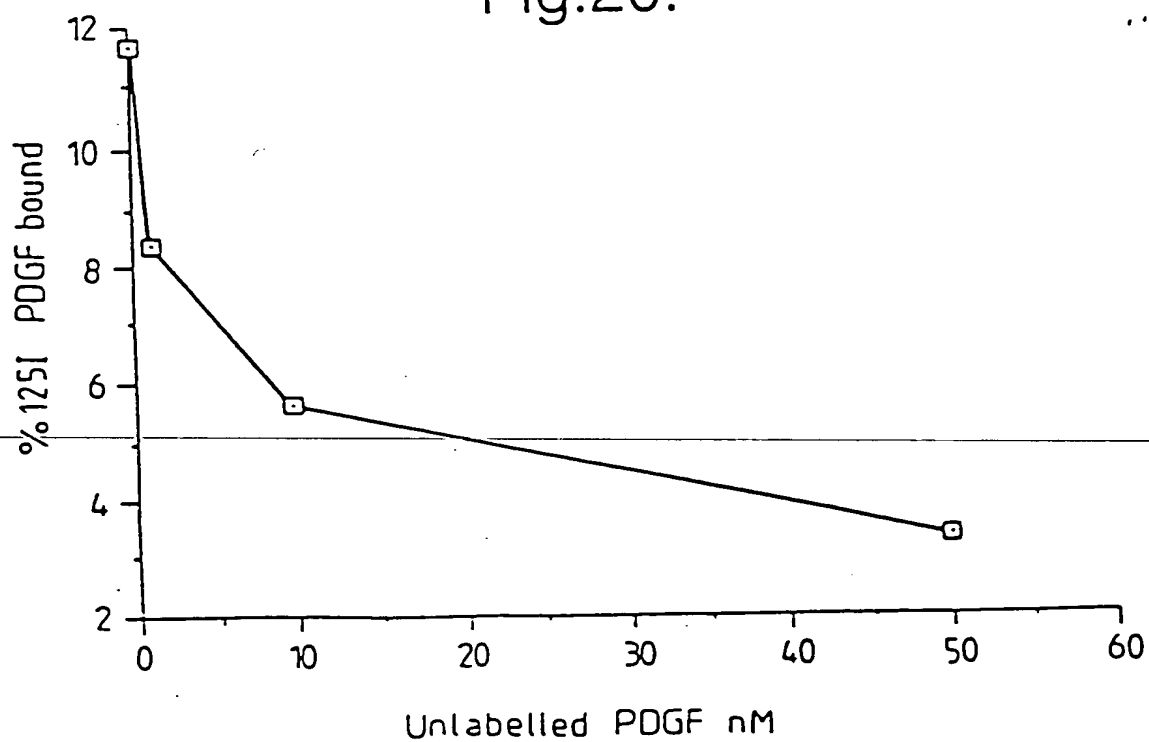


Fig.21.

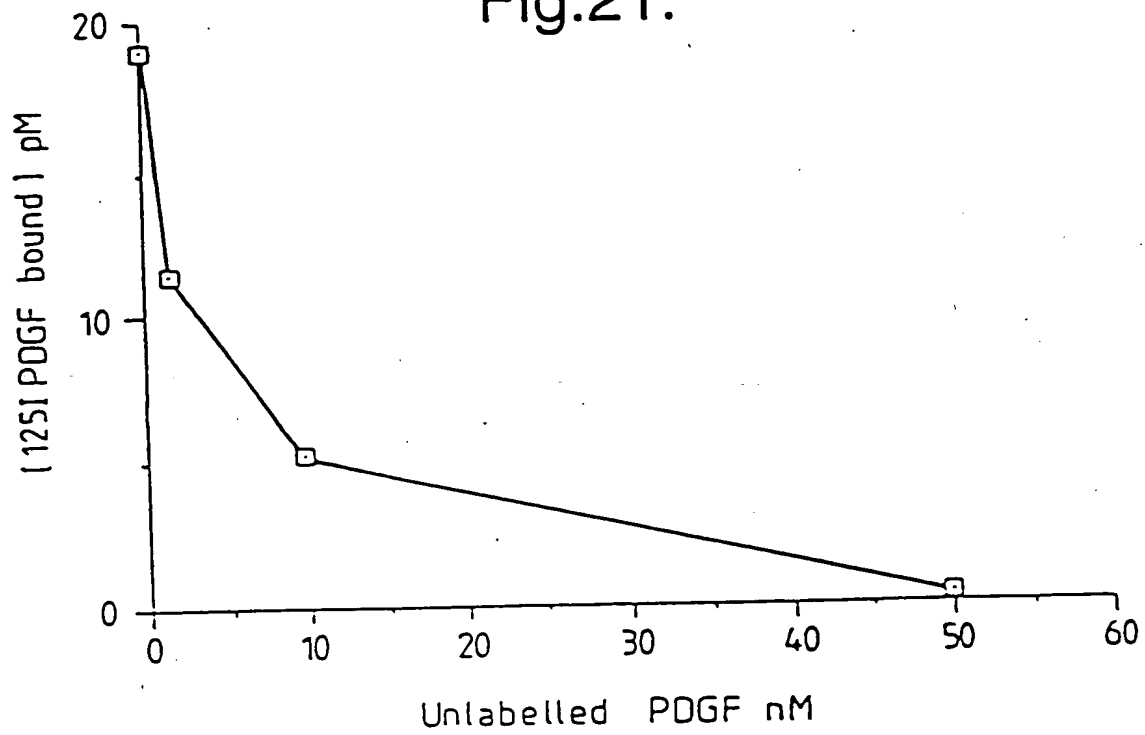


Fig.22.

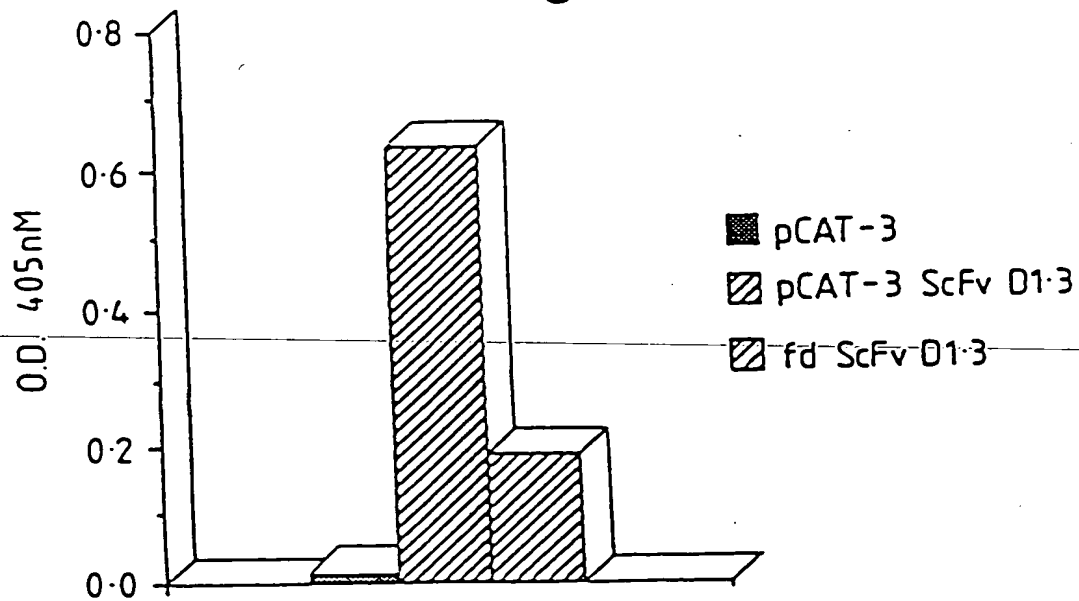


Fig.23( i )

d  
M

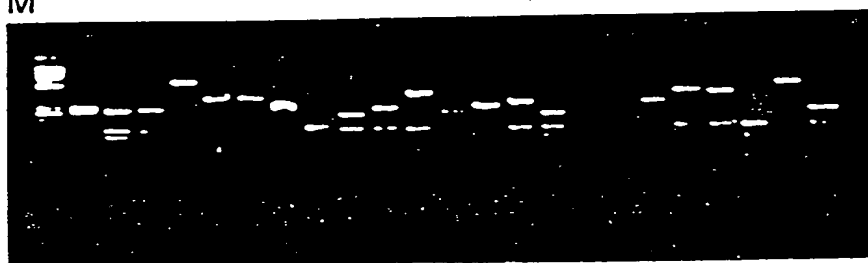
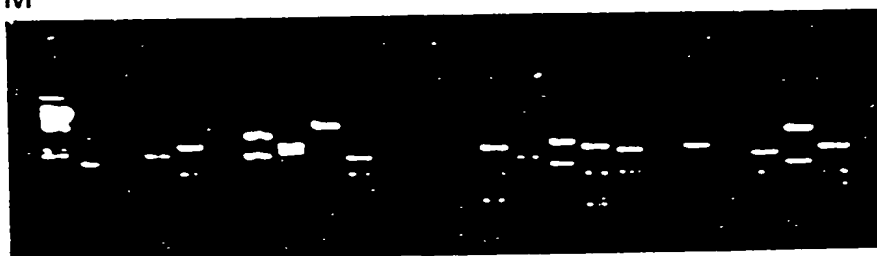


Fig.23(ii)

M



# VH sequences

Fig.24.

from combinatorial library:

	CDR1	CDR2	CDR3							
A	QVQLQSGDAELARPGASVYKSCKASGTTT	ETTHMI	WVKQRPQCGCLEMIG	YINPSGCTYTHNQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVTYCAR	RYGAY	MGCGTTVTVS8	x4	1	(SEQ ID NO. 214)
B	QVRLQSGDAELAKPGASVYKSCKASGTTT	RDTHMI	MLKQRPQCGCLEMIG	YINPSTGCTYTHNQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVTYCAR	NYGLY	MGCGTTVTVS8	x9	1	(SEQ ID NO. 215)
C	QVQLQSGDAELVYKPGASVYKSCKASGTTT	STYTHMI	WVKQRPQCGCLEMIG	YINPSTGCTYTHNQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVTYCAR	YRSPFY	MGCGTTVTVS8	x3	1	(SEQ ID NO. 216)
D	QVQLQSGDAELVYKPGASVYKSCKASGTTT	GYTHMI	WVKQSHGSKLELMIG	RINPYNODT YTHNQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVTYCAR	ITTRFAY	MGCGTTVTVS8	x3	1	(SEQ ID NO. 217)
E	QVQLQSGDAELVYKPGASVYKSCKASGTTT	SYGVH	WVKQRPQCGCLEMIG	VINAGGSTRYHNSALHS	RLSISKDNSSQVFLNQLSLQTDYTDYTHNQKFKD	URGDY	MGCGTTVTVS8	2	1	(SEQ ID NO. 218)
F	QVQLQSGDAELVYKPGASVYKSCKASGTTT	STLTHMI	WVKQRPQCGCLEMIG	YINPSTGCTYTHNQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVTYCAR	DYGY	MGCGTTVTVS8	1	1	(SEQ ID NO. 219)
G	QVRLQSGDAELVYKPGASVYKSCKASGTTT	RYLTHMI	WVKQRPQCGCLEMIG	YINPSTGCTYTHNQKFKD	ENTLTADKSSSTA YHQLSSLTSEDSAVTYCAR	DYGY	MGCGTTVTVS8	1	1	(SEQ ID NO. 220)
H	QVQLQSGDAELVYKPGASVYKSCKASGTTT	RUTTHMI	WVKQSHGSKLELMIG	YINPSTGCTYTHNQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVTYCAR	DYGRD	MGCGTTVTVS8	1	1	(SEQ ID NO. 221)

from hierarchical library VH-sep x Vc-d:

I	QVRLQSGDAELARPGASVYKSCKASGTTT	STYTHMI	WVKQSHGKSLLEMIG	YINPSTGCTYTHNQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVTYCAR	DYGRD	MGCGTTVTVS8	1	1	(SEQ ID NO. 222)
J	QVRLQSGDAELARPGASVYKSCKASGTTT	RYTHMI	WVKQRPQCGCLEMIG	YINPSTGCTYTHNQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVTYCAR	DRGAY	MGCGTTVTVS8	1	1	(SEQ ID NO. 223)
K	QVRLQSGDAELARPGASVYKSCKASGTTT	RDTHMI	WVKQRPQCGCLEMIG	YINPSTGCTYTHNQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVTYCAR	NYGLY	MGCGTTVTVS8	x3	1	(SEQ ID NO. 224)
L	QVQLQSGDAELARPGASVYKSCKASGTTT	NYLTHMI	WVKQRPQCGCLEMIG	YINPSTGCTYTHNQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVTYCAR	DYGY	MGCGTTVTVS8	x2	1	(SEQ ID NO. 225)
M	QVQLQSGDAELARPGASVYKSCKASGTTT	NYTHMI	WVKQRPQCGCLEMIG	YINPSTGCTYTHNQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVTYCAR	DYGY	MGCGTTVTVS8	1	1	(SEQ ID NO. 226)
N	QVQLQSGDAELARPGASVYKSCKASGTTT	STYTHMI	WVKQRPQCGCLEMIG	YINPSTGCTYTHNQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVTYCAR	DYGY	MGCGTTVTVS8	1	1	(SEQ ID NO. 227)
O	QVQLQSGDAELARPGASVYKSCKASGTTT	STLTHMI	WVKQRPQCGCLEMIG	YINPSTGCTYTHNQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVTYCAR	DYGY	MGCGTTVTVS8	1	1	(SEQ ID NO. 228)
P	QVQLQSGDAELARPGASVYKSCKASGTTT	STYTHMI	WVKQRPQCGCLEMIG	YINPSTGCTYTHNQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVTYCAR	DYGY	MGCGTTVTVS8	1	1	(SEQ ID NO. 229)
Q	QVQLQSGDAELARPGASVYKSCKASGTTT	STYTHMI	WVKQRPQCGCLEMIG	YINPSTGCTYTHNQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVTYCAR	DYGY	MGCGTTVTVS8	1	1	(SEQ ID NO. 230)
R	QVQLQSGDAELARPGASVYKSCKASGTTT	STYTHMI	WVKQRPQCGCLEMIG	YINPSTGCTYTHNQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVTYCAR	DYGY	MGCGTTVTVS8	1	1	(SEQ ID NO. 231)
S	QVQLQSGDAELARPGASVYKSCKASGTTT	STYTHMI	WVKQRPQCGCLEMIG	YINPSTGCTYTHNQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVTYCAR	DYGY	MGCGTTVTVS8	1	1	(SEQ ID NO. 232)
T	QVQLQSGDAELARPGASVYKSCKASGTTT	STYTHMI	WVKQRPQCGCLEMIG	YINPSTGCTYTHNQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVTYCAR	DYGY	MGCGTTVTVS8	1	1	(SEQ ID NO. 233)
U	QVQLQSGDAELARPGASVYKSCKASGTTT	STYTHMI	WVKQRPQCGCLEMIG	YINPSTGCTYTHNQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVTYCAR	DYGY	MGCGTTVTVS8	1	1	(SEQ ID NO. 234)
V	QVQLQSGDAELARPGASVYKSCKASGTTT	STYTHMI	WVKQRPQCGCLEMIG	YINPSTGCTYTHNQKFKD	KATLTADKSSSTA YHQLSSLTSEDSAVTYCAR	DYGY	MGCGTTVTVS8	1	1	(SEQ ID NO. 235)

# Fig.24 (Cont).

## Vx sequences

from combinatorial library:

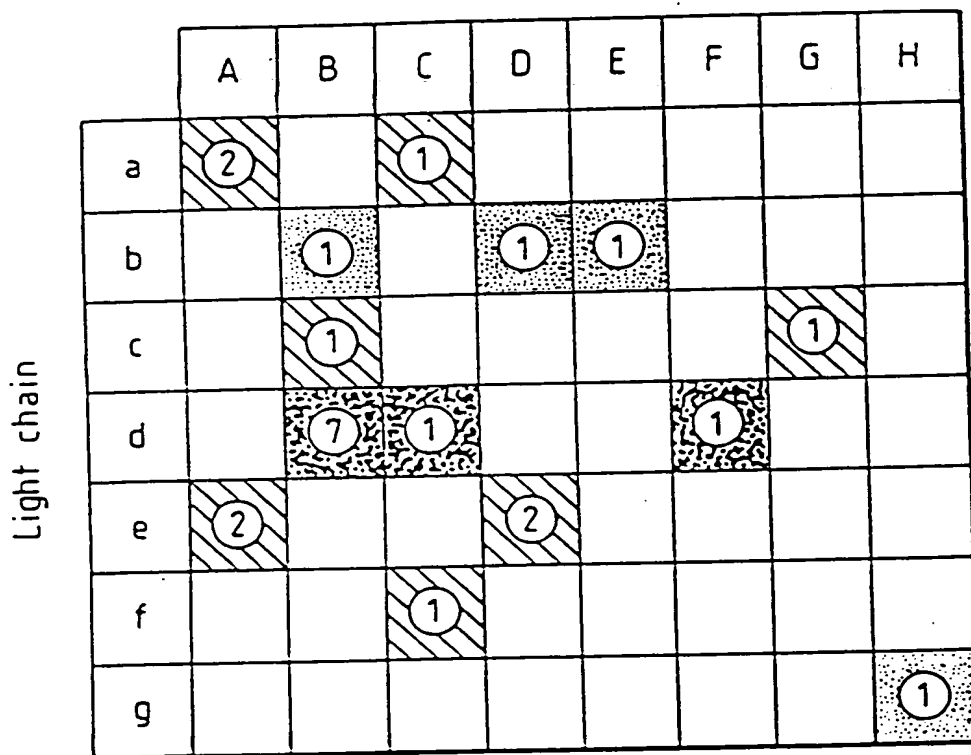
	CDR1	CDR2	CDR3		
a	RASQELSGTSL	WLOQRPGDSIKRLIY	LOYASYPT	FCAGTKLEIKRA X3	ox-1like (SEQ ID NO. 236)
b	RASSSV66SYLH	MYQOKSGASPKVMIIY	QQYSGYPLT	FCAGTKLEIKRA X3	ox-1like (SEQ ID NO. 237)
c	SASSS16SNYLH	MYQOKPGFSPKLLIY	QQGSS1PLT	FCAGTKLEIKRA X3	ox-1like (SEQ ID NO. 238)
d	SASSS16SNYLH	MYQOKPGFSPKLLIS	QQGST1PFT	FG9GTKLEIKRA X9	ox-1like (SEQ ID NO. 239)
e	SASSSVNTTH	MYQOKPGTSPKLMIIY	QQRSYPT	FGSOTKLEIKRA X4	ox-1like? (SEQ ID NO. 240)
f	SASSSVSTN	MYQOKSGTSPKRMIIY	QQFSN1PLT	FCAGTKLEIKRA	Vtox1 (SEQ ID NO. 241)
g	SASSS1NTH	MYQOKPGASPKRMIIY	IQNRSYPT	FGGTKLEIKRA	ox-1like? (SEQ ID NO. 242)

from hierarchical library VII-B x Vx-rep:

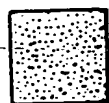
h	SASSSVSTN	DTSKLAS	QQMSN1PLT	FCAGTKLEIKRA X4	Vtox1 (SEQ ID NO. 243)
i	SASSSVETIH	STSNLAS	QQTHSYPLT	FCAGTKLEIKRA	ox-1like? (SEQ ID NO. 244)
j	SASSS1SSNYLH	RTSNLAS	QQGSS1PLT	FCGGTKLEIKRA	ox-1like (SEQ ID NO. 245)
k	SATS61SSNYLH	RTSNLAS	QQGSS1PFT	FCAGTKLEIKRA	ox-1like (SEQ ID NO. 246)
l	SASSS1SSNYLH	RTSNLAS	QQGSS1PFT	FCGGTKLEIKRA	ox-1like (SEQ ID NO. 247)
m	SASSS1SSNYLH	RTSNLAS	QQGSS1PFT	FCGGTKLEIKRA	ox-1like (SEQ ID NO. 248)
n	SASSS1SSNYLH	RTSNLAS	QQGSS1PFT	FCGGTKLEIKRA	ox-1like (SEQ ID NO. 249)
o	SASSSVSTN	RTSNLAS	QQGSS1PFT	FCGGTKLEIKRA X3	ox-1like (SEQ ID NO. 250)
p	SASSSVSTN	DTSKLAS	QQMSN1PLT	FCAGTKLEIKRA X3	Vtox1 (SEQ ID NO. 251)
q	SASSSVSTN	DTSKLAS	QQMSN1PLT	FCGGTKLEIKRA	Vtox1 (SEQ ID NO. 252)
r	SASSSVSTN	DTSKLAS	QQMSN1PLT	FCAGTKLEIKRA	Vtox1 (SEQ ID NO. 253)
s	RASSSVT6YLH	STSNLAS	QQYSGYPLT	FCAGTKLEIKRA	ox-1like (SEQ ID NO. 254)
t	RASSSV66SYLH	STSNLAS	QQRSYPLT	FCAGTKLEIKRA	ox-1like (SEQ ID NO. 255)
u	RASSSV66SYLH	STSNLAS	QQYSGYPLT	FCAGTKLEIKRA	ox-1like (SEQ ID NO. 256)
v	RASSSV66SYLH	STSNLAS	QQYSGYPLT	FCGGTKLEIKRA	ox-1like (SEQ ID NO. 257)
w	SASSS1SSNYLH	RTSNLAS	QQGSS1PFT	FCAGTKLEIKRA X3	ox-1like (SEQ ID NO. 258)

# Fig.25.

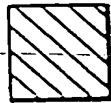
HEAVY CHAIN



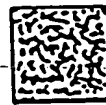
OD<sub>405nm</sub> in ELISA



0.2-0.9



0.9-2.0



>2.0



Fig.26(a).

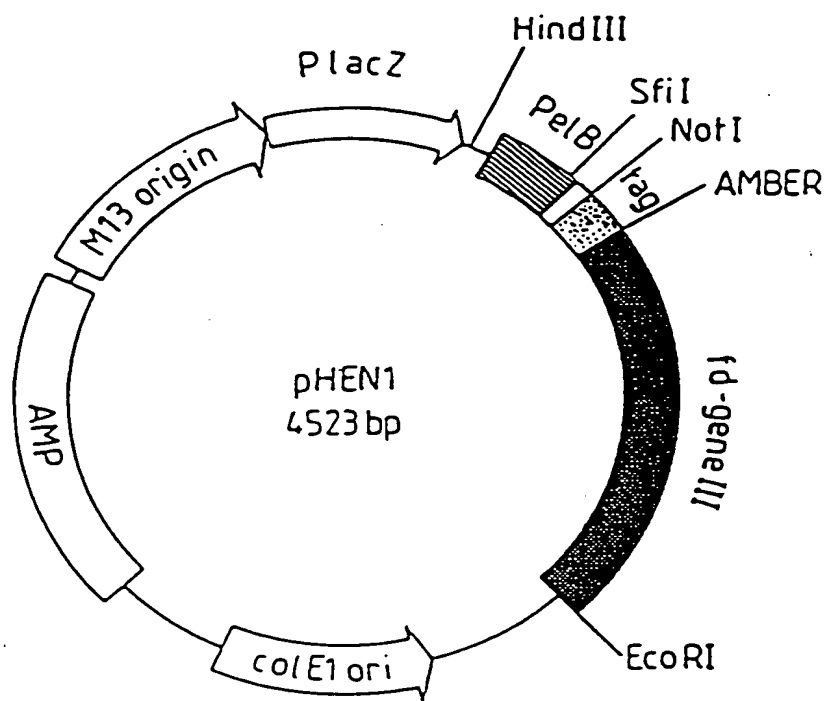


Fig.26(b).

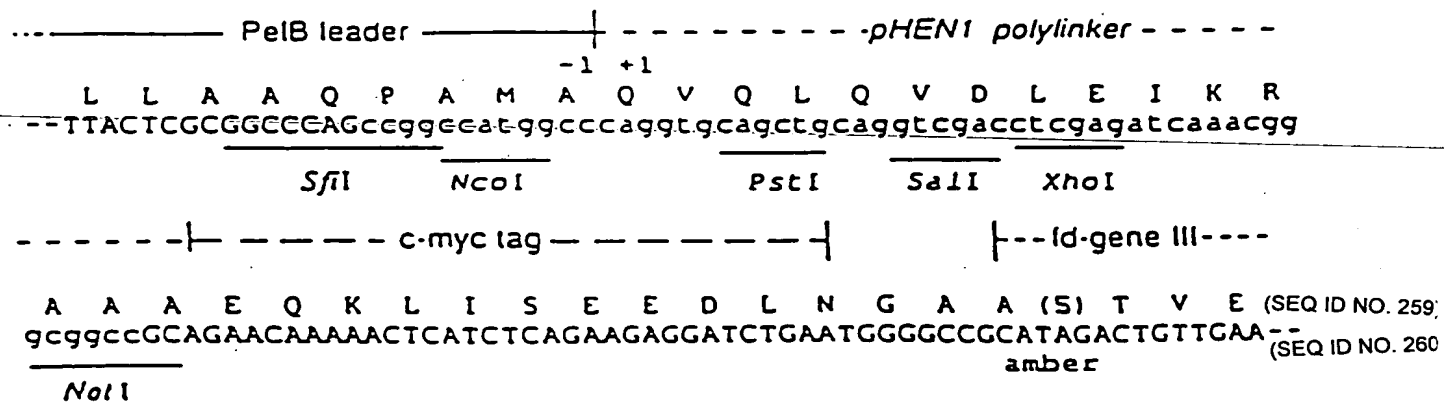


Fig.27.

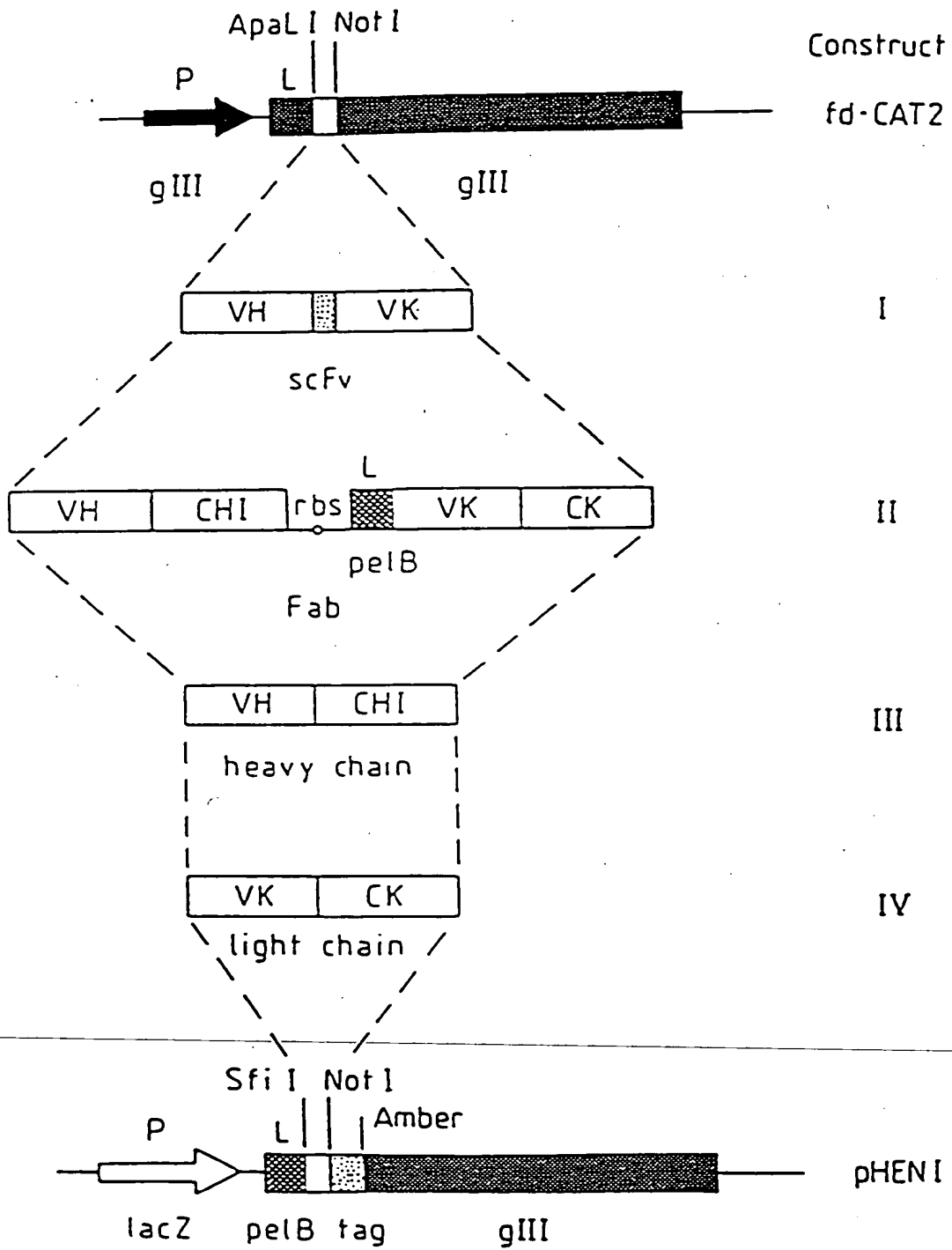
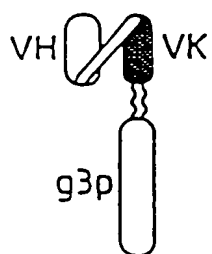
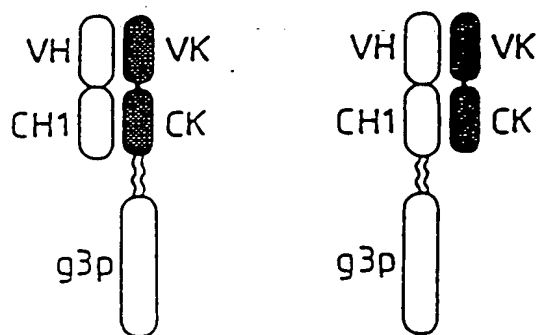


Fig.28.

Fab



scFv

Fig.29.

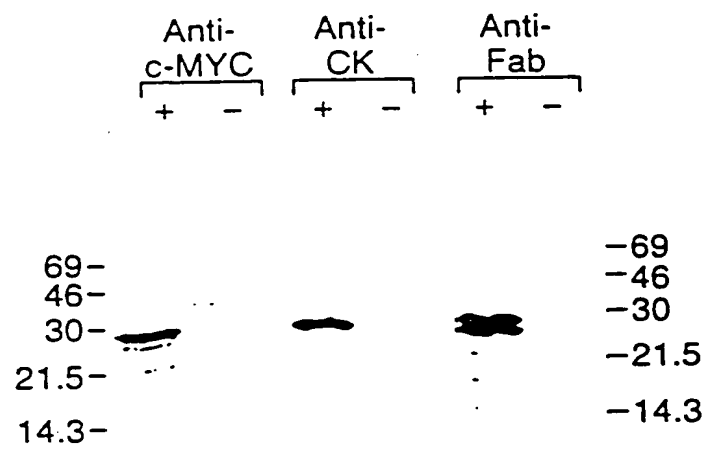


Fig.30.

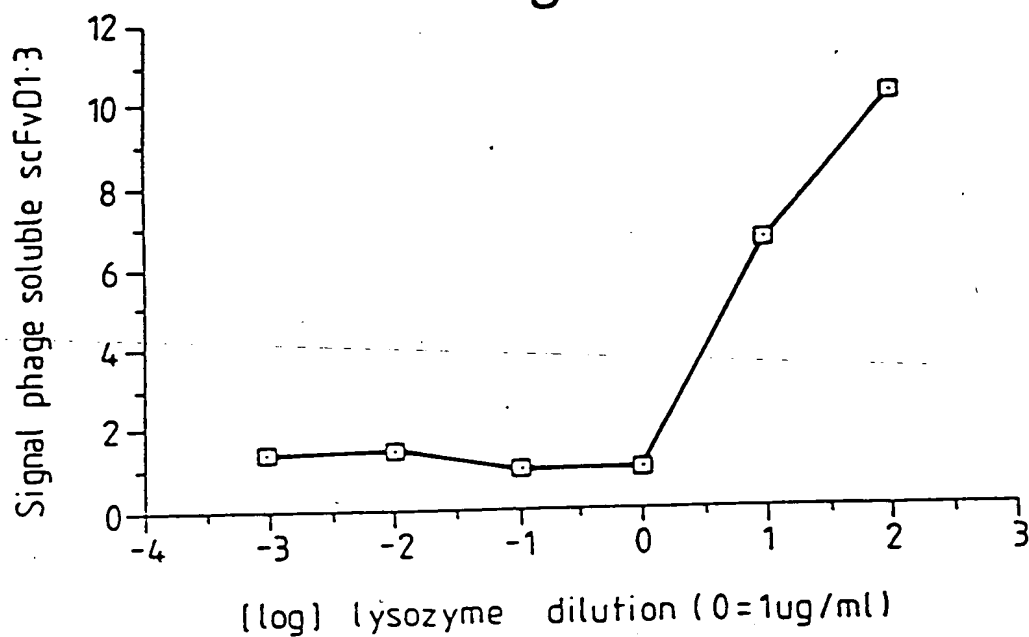


Fig.31.

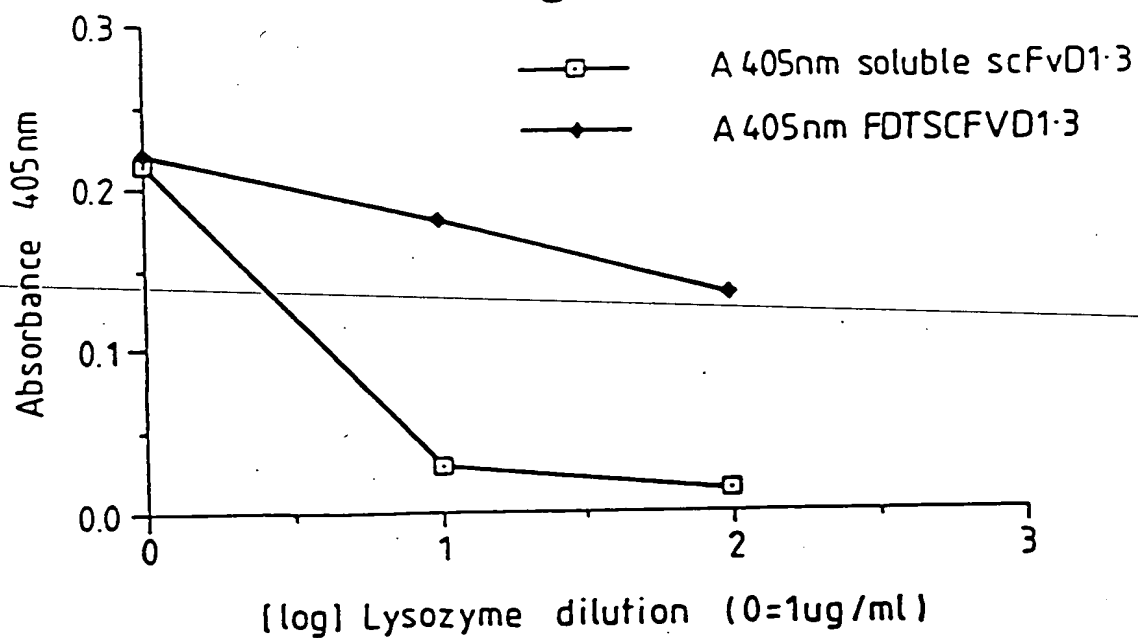


Fig.32.

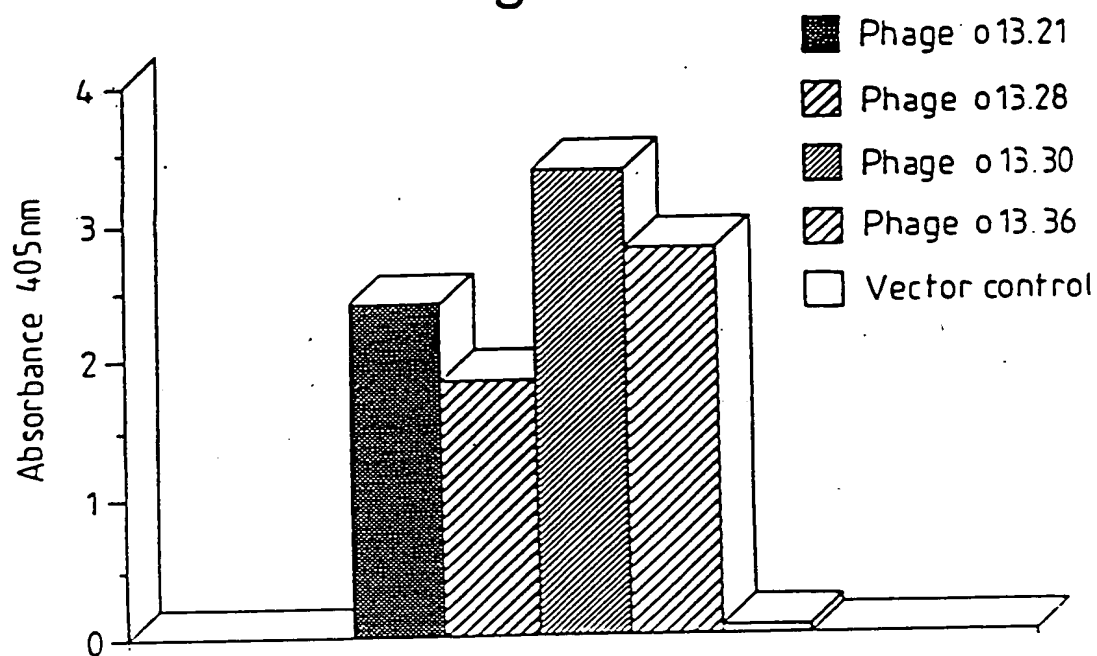


Fig.33.

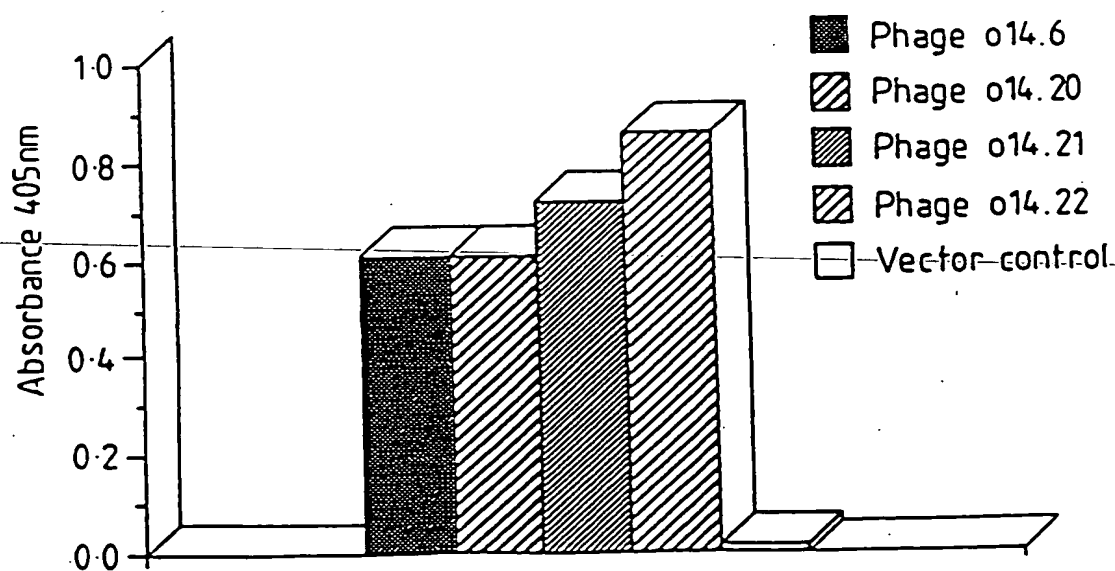


Fig.34.

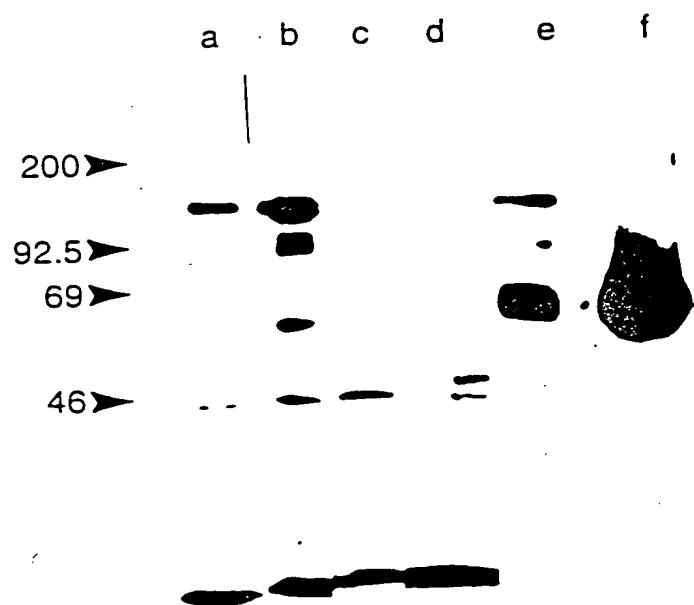


Fig.35A.

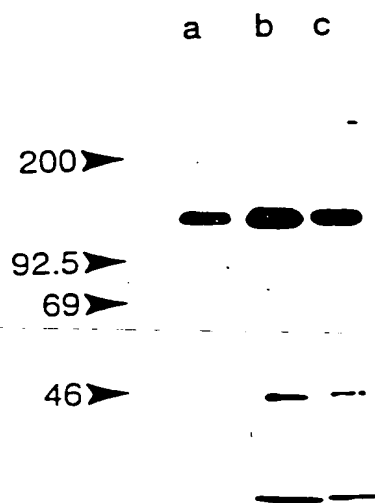


Fig.35B.

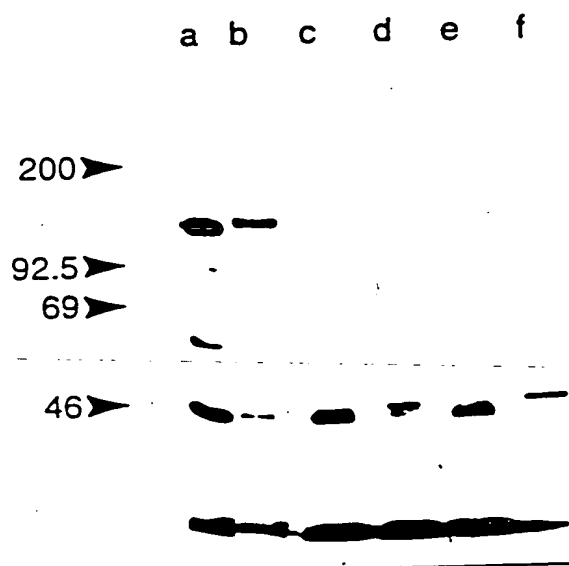


Fig.36.

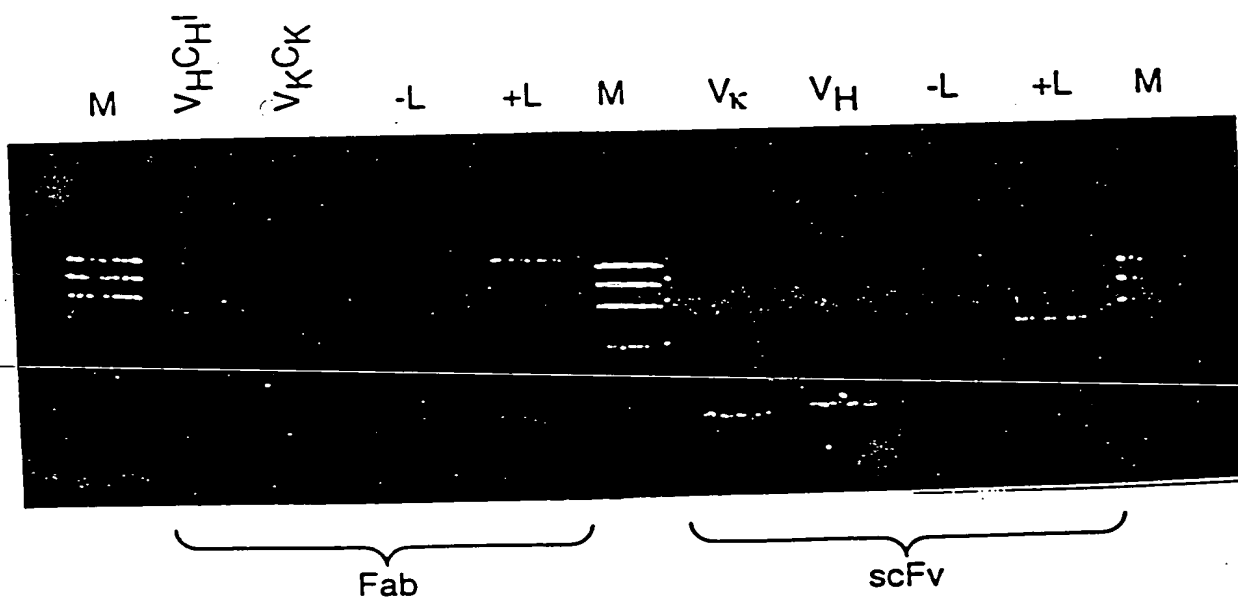




Fig.37.

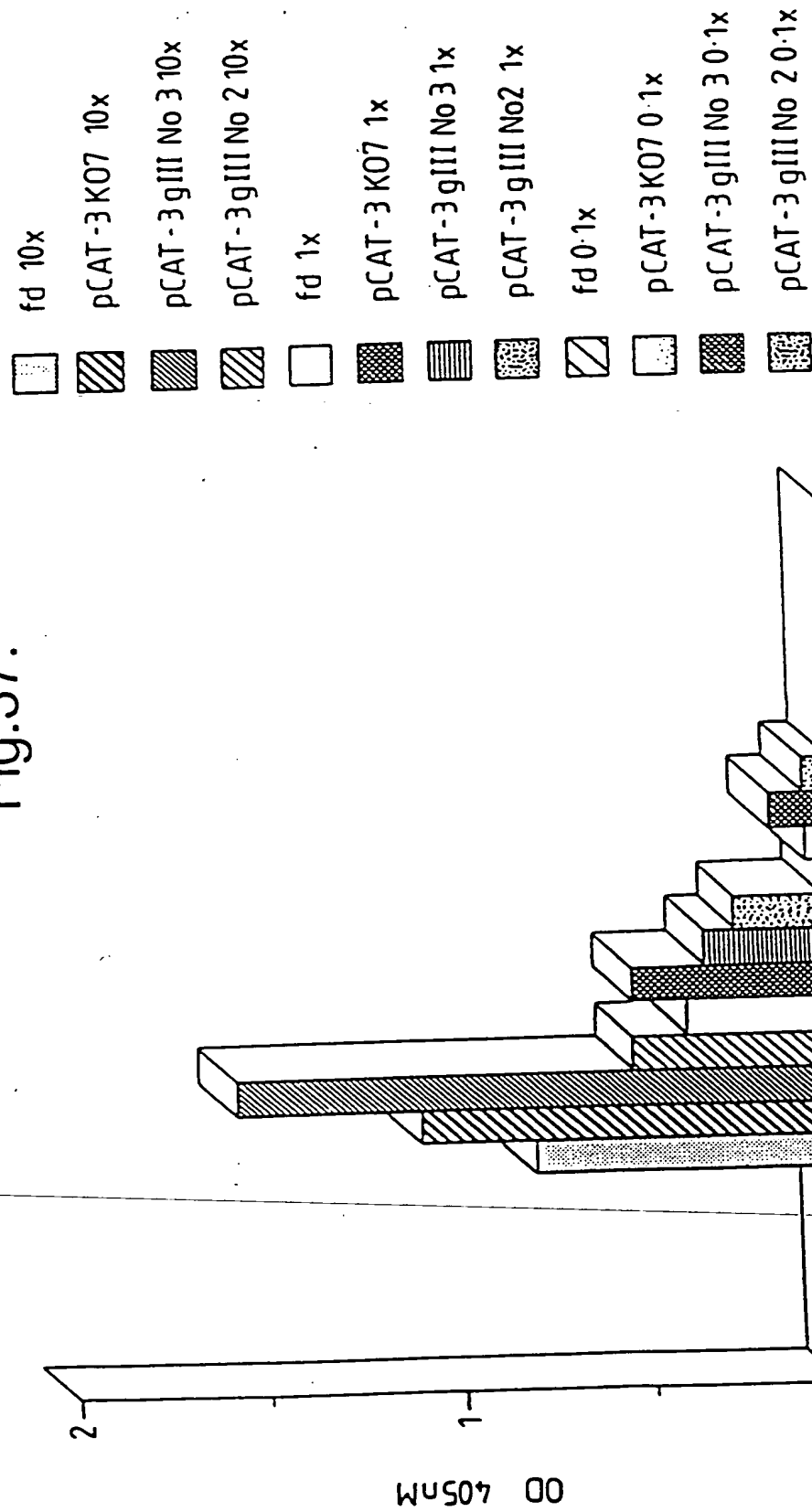


Fig.38A.



Fig.38B.

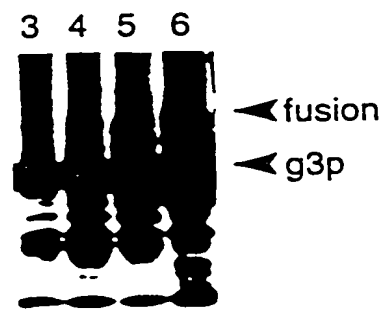


Fig.39.

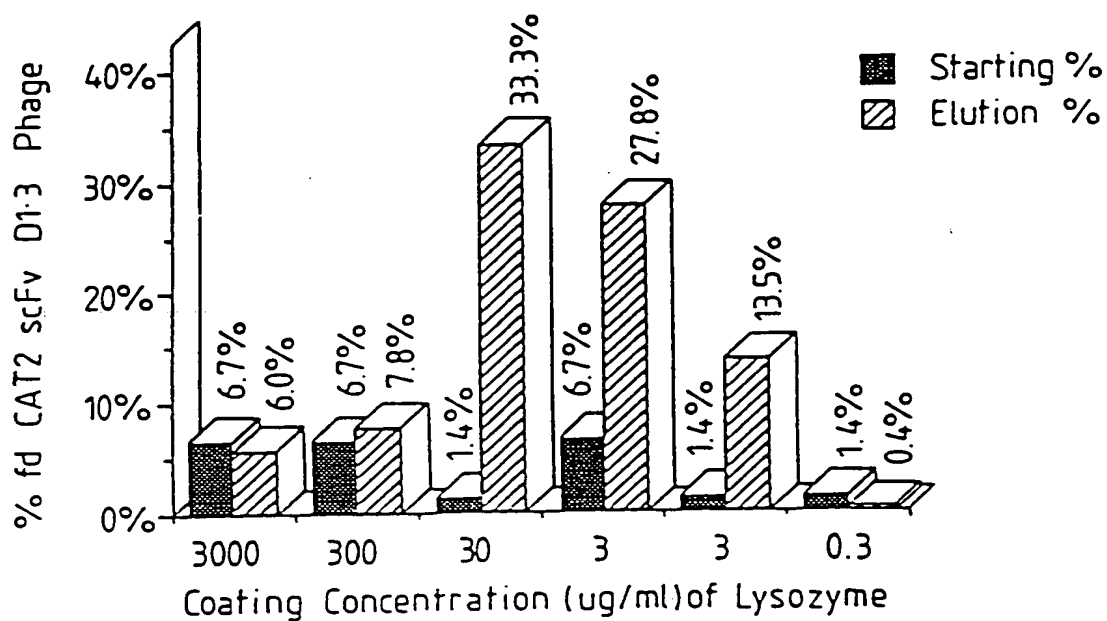


Fig.40.

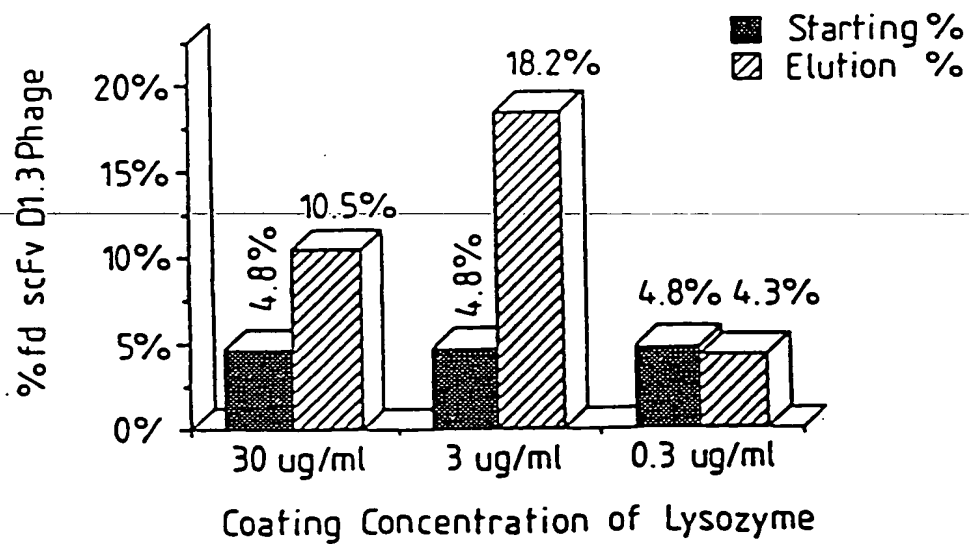


Fig.41.

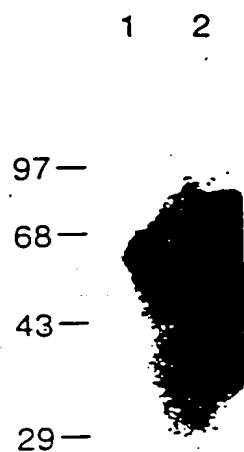


Fig.42.

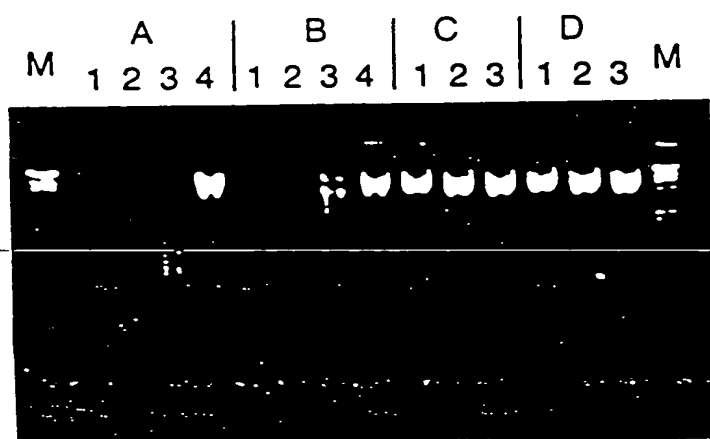


Fig.43.

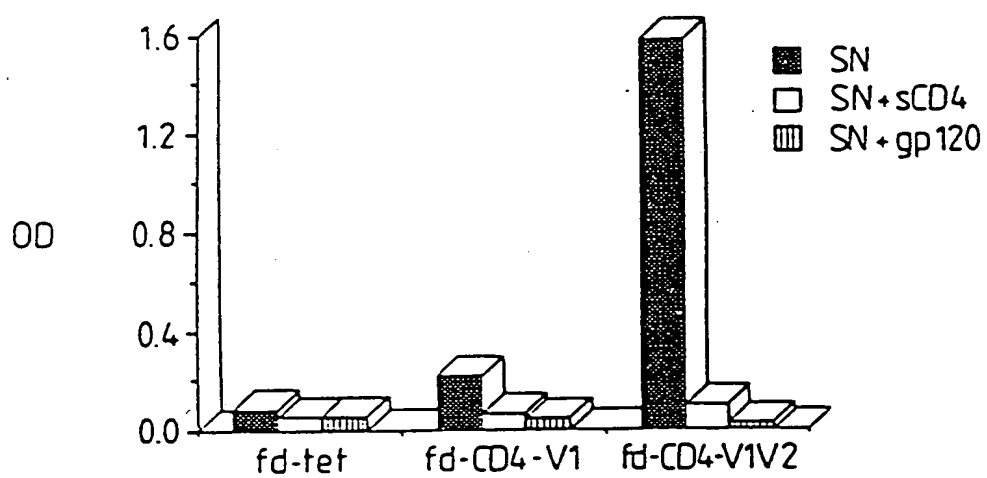


Fig.44 (i).

10	20	30	40	50	60	70	80	90
TTCTATTCTACAGTGCNAGGTC	CAGCTGCAGCAGTCTGGGGCT	GAGCTTGTGAAGCCTGGGGCT	TCAGTGAAGCTGTCTCTGCAAGGCT					
AAGATAAGAGTGTACGTCTCAGG	TCGACGTCGACACCTCGAACAC	ACTTCGGACCCCGAAGTCACTTC	GACAGGACGCTTCCGA					
PheTyrSerHisSerAlaGlnVal	GlnLeuGlnSerGlyAlaGluLeu	VallysProGlyAlaSerVallysLeu	SerCysLysAla					
100	110	120	130	140	150	160	170	180
TCTGGCTACACCTTCACCAGCTA	CTGGATGCACCTGGGTGAAGCAG	AGGCCCTGGACGAGGCCCTTGAG	TGGATTGGAGGATTGATCCTTAAT					
AGACCGATGTGGAGTGGTCGATG	ACCTACGTGACCCACTTCGTCTC	CGGACCTGCTCCGGAACCTCAC	CTAACCTTCTCTAAGGATTA					
SerGlyTyrThrPheThrSerTyr	TrpMetHisTrpVallysGlnArg	ProGlyArgGlyLeuGluTrpIle	GlyArgIleAspProAsn					
190	200	210	220	230	240	250	260	270
AGTGGTGGTACTAAGTACANTG	AGAGCAAGGCCACACTGACTGT	AGACNAACCCCTCCAGCACAGC	CTACATGCAGCTCAGC					
TCACCACCATGATTCATGTTACT	CTCTCAAGTCTCGTTCGGGTG	TGACTGACATCTGTTGGGAGG	TCGTGTCGGATGTACGTCGAGTCG					
SerGlyGlyThrLysTyrAsnGlu	LysPheLysSerLysAlaThrLeu	ThrValAspLysProSerSerThr	AlaTyrMetGlnLeuSer					
280	290	300	310	320	330	340	350	360
AGCCTGACATCTGAGGACTCTG	CGGTCTATTATTGTGAGN	TACGACTACGCTACTTGTACT	ACTTGTGACTGCGGCCAAGGGACC					
TCGGACTGTAGACTCCTGAGAC	CGCCAGATAATAACACGTTCT	TATGCTGATGCCATCATCGATG	ATGAACTGATGACCCCGGTTCCCTGG					
SerLeuThrSerGluAspSerAla	ValTyrTyrCysAlaArgTyr	AspTyrGlySerSerTyrTyrPhe	AspTyrTrpGlyGlnGlyThr					
370	380	390	400	410	420	430	440	450
ACGGTCACCGTCTCCTCNGGTG	GAGCGGTTTCAGGCGGAGGTG	GCTCTGGCGGTGGCGGATCC	CAGGCTGTTGGGACACAGGAATCTGCA					
TGCCAGTGGCAGAGGAGTCCAC	CTCCGCCAAGTCCGCCCTCC	ACCGAGACCGCCACCGCTAG	GGTCCGACAAACCCCTGTGTCTTAGACGT					
ThrValThrValSerSerGlyGly	GlySerGlyGlyGlySerGly	GlyGlyGlyGlyGlyGlyGly	AlaValGlyThrGlnGluSerAla					
460	470	480	490	500	510	520	530	540
CTCACCATCACCTGGTGAAAC	AGTCACACTCACTTGTGCTC	CAAGTACTGGGGCTGTTAC	AACTAGTAACACTGCCAACTGGGTCCAA					
GAGTGGTGTAGTGGACCACTT	TGTGAGTGTGAGTGAACAG	CGAGTTTCATGACCCCGACA	AATGTTGATCATGATACGGTTGACCCAGGTT					
LeuThrThrSerProGlyGluThr	ValThrValThrLeuThrCys	ArgSerSerThrGlyAlaValThr	SerAsnTyrAlaAsnTrpValGln					
550	560	570	580	590	600	610	620	630
GAAAACCATCATTTTATTCAC	TGGTCTAATAGGTGGTACCA	ACAACCGAGCTCCAGGTGTT	CTCTGCCAGATTCTCAGGCTCCCTGATT					
CTTTTGGTCTAGTAAATAAGT	GACCAAGATTATCCACCATG	GTGTTGGCTCGAGGTCCACA	AGGACCGTCTAAGAGTCCGAGGACTAA					
GluLysProAspHisLeuPheThr	GlyLeuIleGlyGlyThrAsn	AsnArgAlaProGlyValPro	AlaArgPheSerGlySerLeuIle					

Fig.44 (ii).

640	650	660	670	680	690	700	C	G	710	720
GGAGACAAGGCTGCCCCC	TCACACAGGGGCACAGACTGAGGATGAGGC	AAATATATTTCTGTGCTCTATGG	AC	AGCAACCAT	TGGGTG					
CCTCTGTTCCGACGGGAGTGGT	AGTGTCCTCCCGTCTGACTCCTACTCCGTTATATAAGACACGAGATACCATGTCTGTTGGTAACCCAC									
GlyAspLysAlaAlaLeuThrIleThrGlyAlaGlnThrGluAspGluAlaIleTyrPheCysAlaLeuTrpTyrnberAsnHisTrpVal										
730	740	750	760	770						
TTCGGTGAGGAA	CAAACTGACTGTCTCGAGATCAAAACGGGGCGCCGC									
AAGCCACCTCCTTGGTTGACTGACAGGAGCTCTAGTTTGCCCGCGCGCG										
PheGlyGlyThrLysLeuThrValLeuGluIleLysArgAlaAla										

(SEQ ID NO. 261)

(SEQ ID NO. 262)

Fig.45.

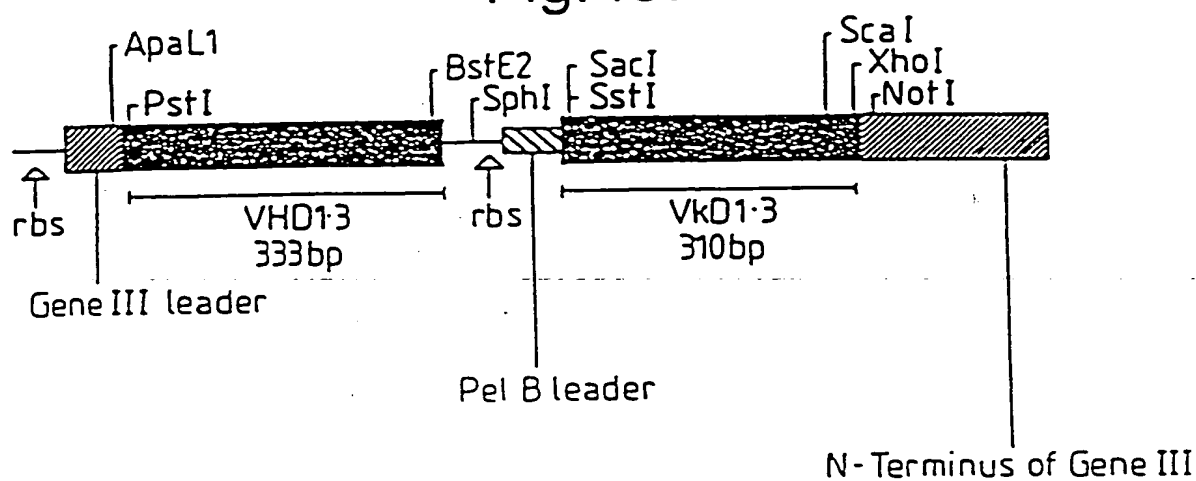


Fig.46.

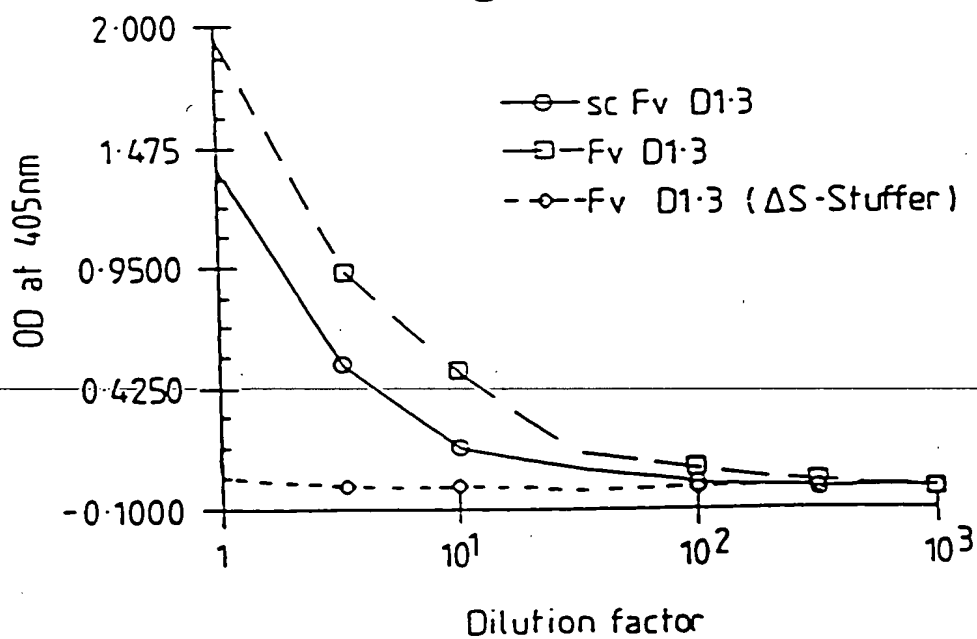




Fig.47.

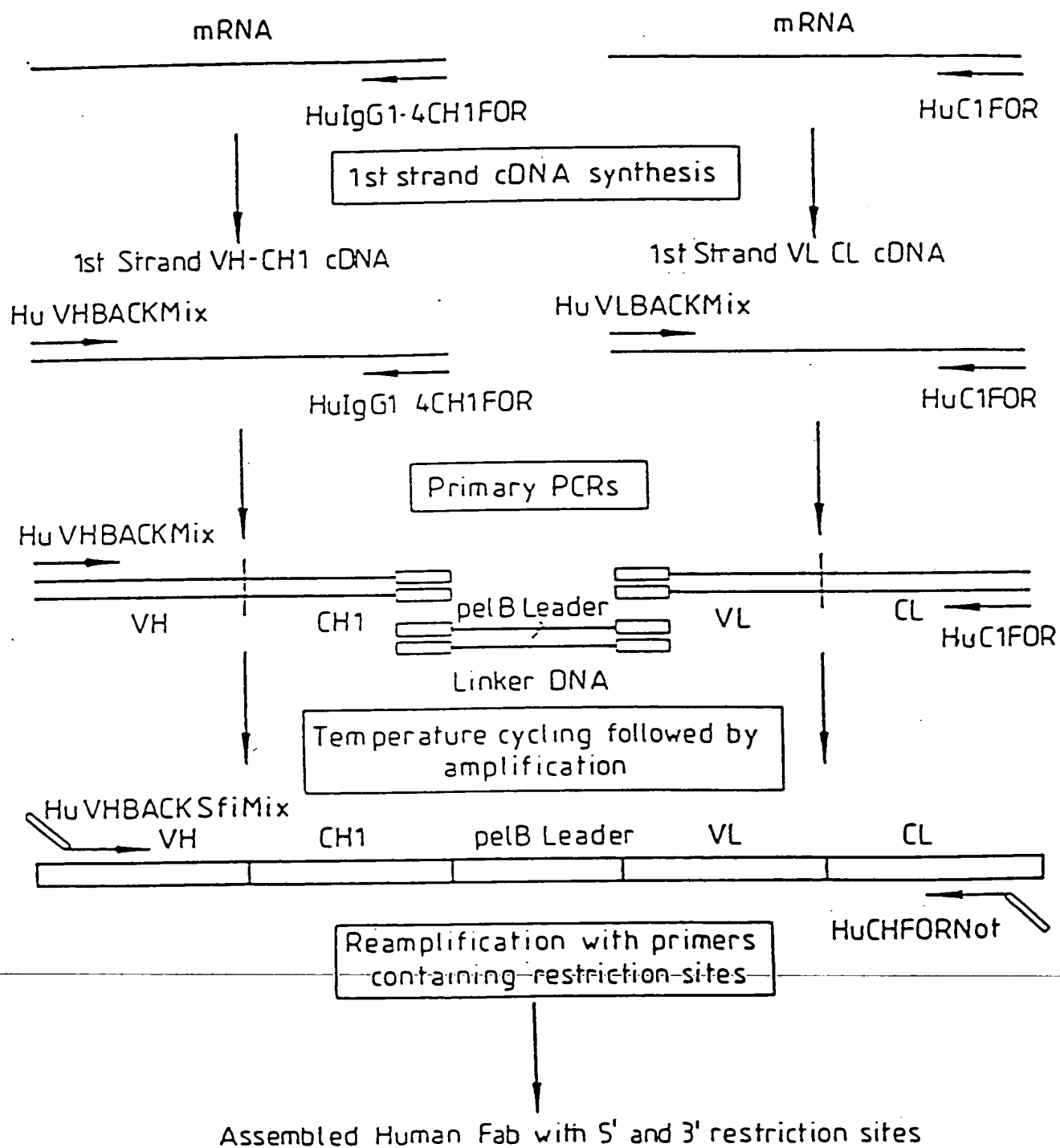


Fig.48(i)

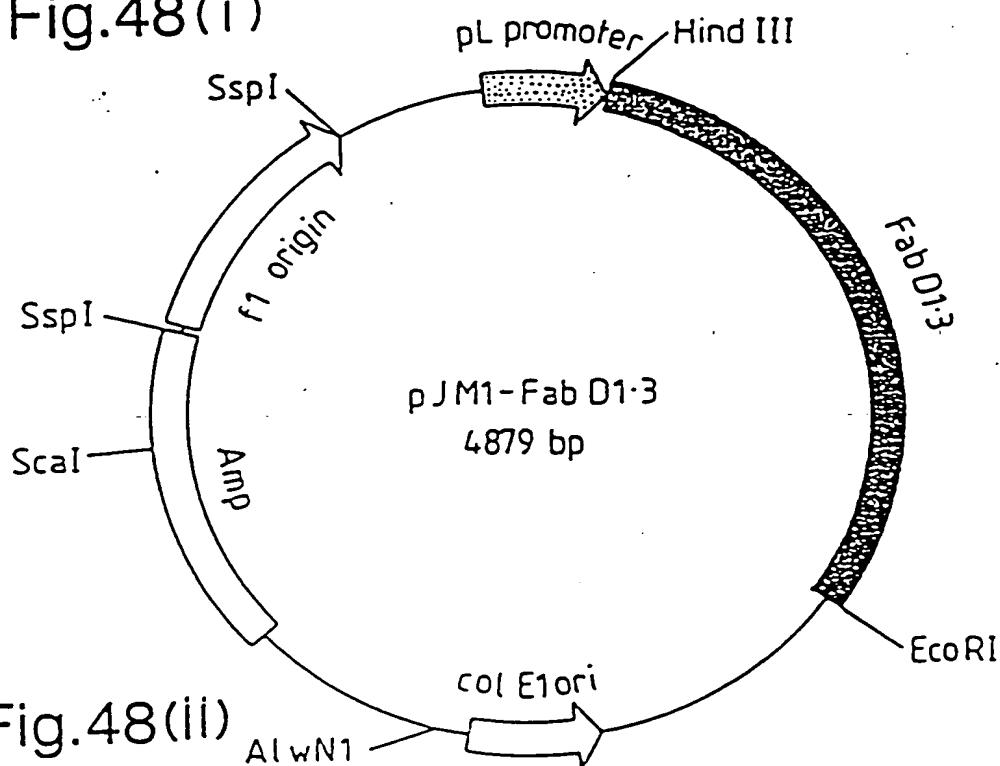


Fig.48(ii)

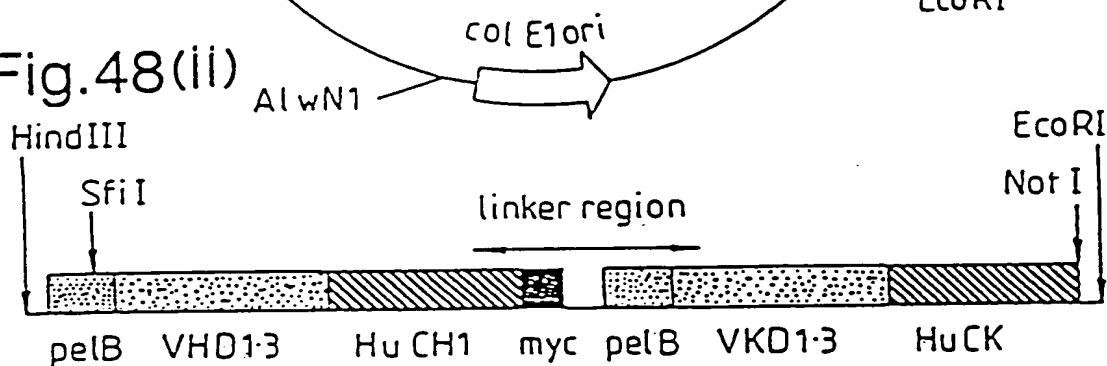


Fig.48(iii)

← 3' Human CH1 and hinge →  
 K P S N T K V D K K V E P K S S T K T H T  
 AACCCAGCAACACCAAGGTCGACAAGAAAGTTGAGCCAAATCTTCAACTAAGACGCACACA

→ myc peptide tag →  
 S G G E Q K L I S E E D L N \* \*  
 TCAGGAGGTGAACAGAAGCTCATCTCAGAGAGATCTGAATTAATAAGGGAGCTTGCATGCA

(SEQ ID NO. 263)

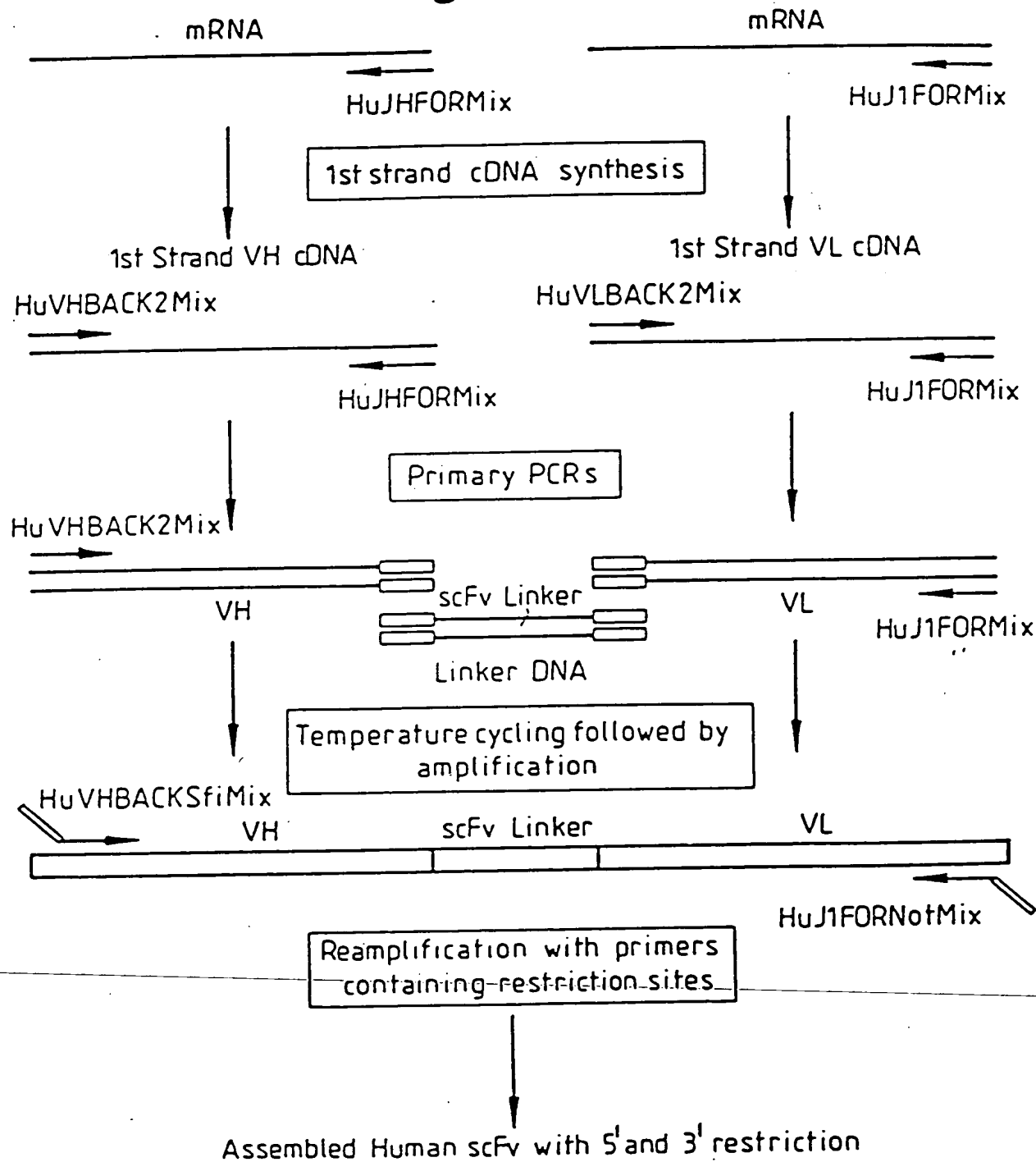
← pelB leader →  
 M K Y L L P T A A A G L  
 AATTCATTTCAAGGAGACAGTCATAATGAATAACCTATTGCTACGGCAGCCGCTGGATTGT

→ 5' Vk →  
 L L P A A Q P A M A D I E L T Q S P  
 TATTAACTGCTGOCOAACCAAGGATGGGACATGAGTTCAACCCAGTCTCC

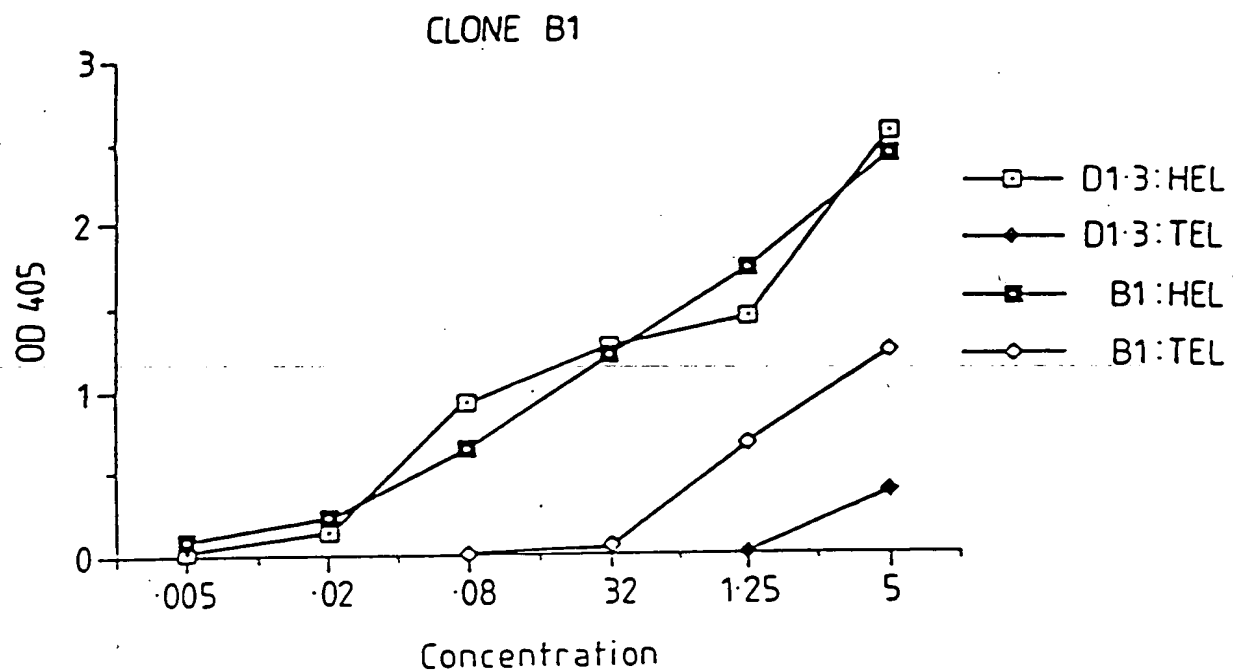
(SEQ ID NO. 264)

(SEQ ID NO. 265)

Fig.49.



# Fig.50(i)



# Fig.50(ii)

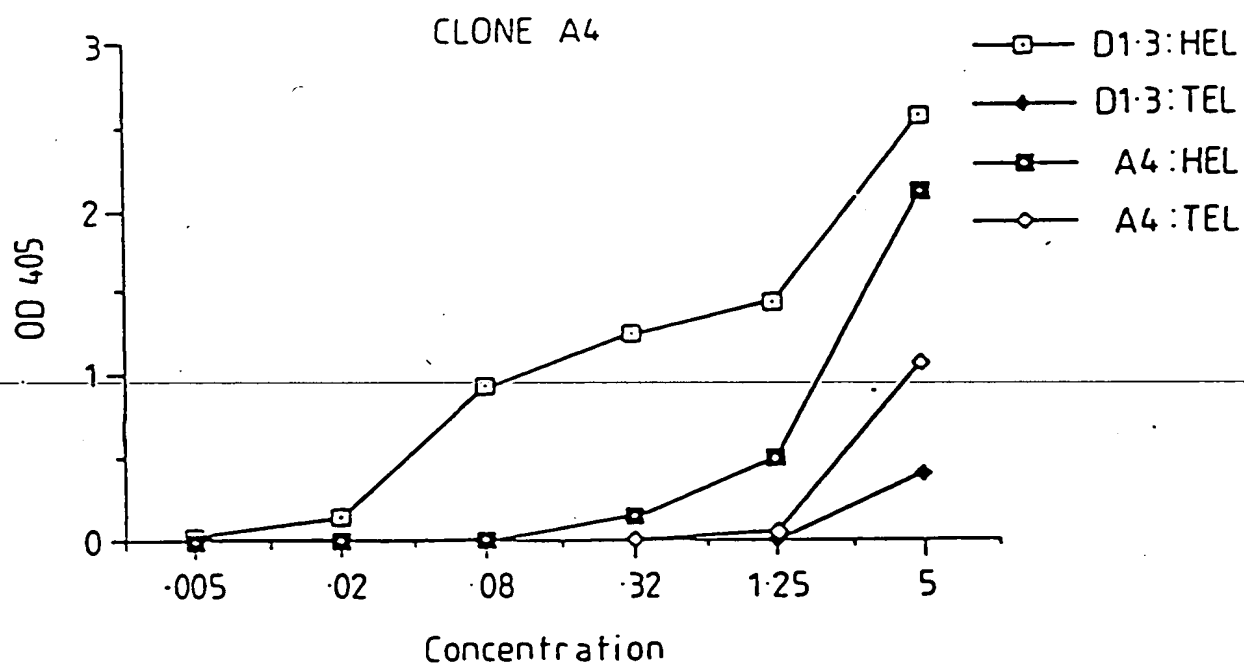


Fig.51.

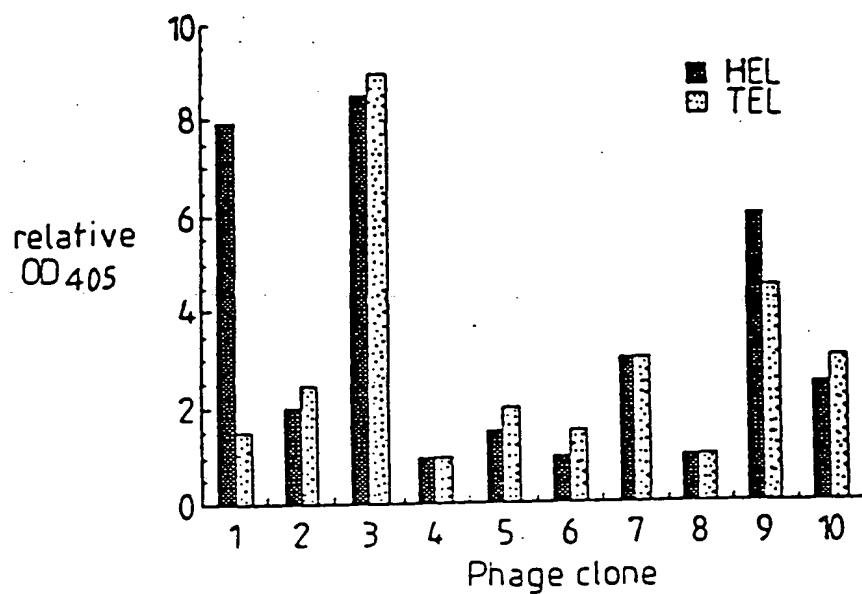


Fig.53.

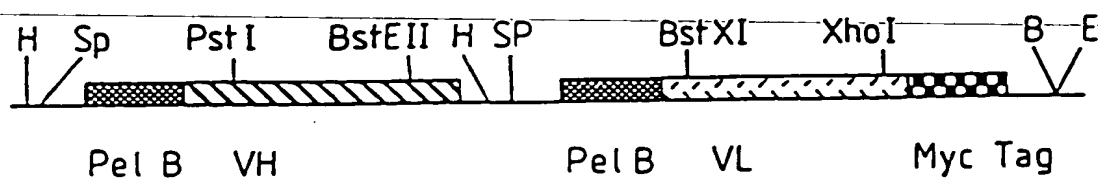


Fig.52.

CDR 1

CDR 2

D1.3 DIQMTQSPASLSASVGETVTITCRASGNIHNYLA WYQQKQKSPQQLLVYYTTLAD  
M1F DIELTQSPSSLASLGERVSLTCRASQDIGSSLN WLQQEPDGTIKRLIYATSSLD S  
M21 DIELTQSPALMAASPGEKVITICSVSSSISSNLHWYQQKSETSPKPIYGTSNLAS

CDR 3

D1.3 GVPSRFSGSGGTQYSLKINSLQPEDFGSYQCQHFWSPTPTFGGGTKLEIKR (SEQ ID NO. 266)  
M1F GVPKRFGSRGSDYSLTISSESEDFVDYVCLQYASSPWTFGGGTKLELKR (SEQ ID NO. 267)  
M21 GVPVRFSGSGGTSLTISSEAEADAATYQCQWSSYP LTFGAGTKLEIKR (SEQ ID NO. 268)